U.S. PUBLIC HEALTH RESPONSE TO THE ZIKA VIRUS: CONTINUING CHALLENGES

HEARING

BEFORE THE

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

OF THE

COMMITTEE ON ENERGY AND COMMERCE

HOUSE OF REPRESENTATIVES

ONE HUNDRED FIFTEENTH CONGRESS

FIRST SESSION

MAY 23, 2017

Serial No. 115–34

Printed for the use of the Committee on Energy and Commerce
energycommerce.house.gov

U.S. GOVERNMENT PUBLISHING OFFICE

26–480 PDF WASHINGTON : 2017

For sale by the Superintendent of Documents, U.S. Government Publishing Office
Internet: bookstore.gpo.gov Phone: toll free (866) 512–1800; DC area (202) 512–1800
Fax: (202) 512–2104 Mail: Stop IDCC, Washington, DC 20402–0001

COMMITTEE ON ENERGY AND COMMERCE

GREG WALDEN, Oregon
Chairman

JOE BARTON, Texas
Vice Chairman
FRED UPTON, Michigan
JOHN SHIMKUS, Illinois
TIM MURPHY, Pennsylvania
MICHAEL C. BURGESS, Texas
MARSHA BLACKBURN, Tennessee
STEVE SCALISE, Louisiana
ROBERT E. LATTA, Ohio
CATHY MCMORRIS RODGERS, Washington
GREGG HARPER, Mississippi
LEONARD LANCE, New Jersey
BRETT GUTHRIE, Kentucky
PETE OLSON, Texas
DAVID B. MCKINLEY, West Virginia
ADAM KINZINGER, Illinois
H. MORGAN GRIFFITH, Virginia
GUS M. BILIRAKIS, Florida
BILL JOHNSON, Ohio
BILLY LONG, Missouri
LARRY BUCSHON, Indiana
BILL FLORES, Texas
SUSAN W. BROOKS, Indiana
MARKWAYNE MULLIN, Oklahoma
RICHARD HUDSON, North Carolina
CHRIS COLLINS, New York
KEVIN CRAMER, North Dakota
TIM WALBERG, Michigan
MIMI WALTERS, California
RYAN A. COSTELLO, Pennsylvania
EARL L. "BUDDY" CARTER, Georgia

FRANK PALLONE, JR., New Jersey
Ranking Member
BOBBY L. RUSH, Illinois
ANNA G. ESHOO, California
ELIOT L. ENGEL, New York
GENE GREEN, Texas
DIANA DEGETTE, Colorado
MICHAEL F. DOYLE, Pennsylvania
JANICE D. SCHAKOWSKY, Illinois
G.K. BUTTERFIELD, North Carolina
DORIS O. MATSUI, California
KATHY CASTOR, Florida
JOHN P. SARBANES, Maryland
JERRY MCNERNEY, California
PETER WELCH, Vermont
BEN RAY LUJÁN, New Mexico
PAUL TONKO, New York
YVETTE D. CLARKE, New York
DAVID LOEBSACK, Iowa
KURT SCHRADER, Oregon
JOSEPH P. KENNEDY, III, Massachusetts
TONY CÁRDENAS, California
RAUL RUIZ, California
SCOTT H. PETERS, California
DEBBIE DINGELL, Michigan

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

TIM MURPHY, Pennsylvania
Chairman

H. MORGAN GRIFFITH, Virginia
Vice Chairman
JOE BARTON, Texas
MICHAEL C. BURGESS, Texas
SUSAN W. BROOKS, Indiana
CHRIS COLLINS, New York
TIM WALBERG, Michigan
MIMI WALTERS, California
RYAN A. COSTELLO, Pennsylvania
EARL L. "BUDDY" CARTER, Georgia
GREG WALDEN, Oregon *(ex officio)*

DIANA DEGETTE, Colorado
Ranking Member
JANICE D. SCHAKOWSKY, Illinois
KATHY CASTOR, Florida
PAUL TONKO, New York
YVETTE D. CLARKE, New York
RAUL RUIZ, California
SCOTT H. PETERS, California
FRANK PALLONE, JR., New Jersey *(ex officio)*

C O N T E N T S

Page

Hon. Tim Murphy, a Representative in Congress from the Commonwealth of Pennsylvania, opening statement 1
Prepared statement 3
Hon. Diana DeGette, a Representative in Congress from the State of Colorado, opening statement 4
Hon. Greg Walden, a Representative in Congress from the State of Oregon, opening statement 5
Prepared statement 7
Hon. Frank Pallone, Jr., a Representative in Congress from the State of New Jersey, opening statement 8
Prepared statement 9

WITNESSES

Timothy M. Persons, Ph.D., Chief Scientist, Government Accountability Office 12
Prepared statement 15
Answers to submitted questions 149
Lyle R. Peterson, M.D., Director, Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention 30
Prepared statement 32
Answers to submitted questions 154
Luciana Borio, M.D., Acting Chief Scientist, Food and Drug Administration ... 41
Prepared statement 43
Answers to submitted questions 163
Anthony S. Fauci, M.D., Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health 54
Prepared statement and slide presentation 56
Answers to submitted questions 167
Rick A. Bright, Ph.D., Director, Biomedical Advanced Research and Development Authority, and Deputy Assistant Secretary, Office of the Assistant Secretary for Preparedness and Response, Department of Health and Human Services 77
Prepared statement 79
Answers to submitted questions 172

SUBMITTED MATERIAL

Subcommittee memorandum 121
Letter of February 15, 2017, from Ms. Schakowsky, et al., to Robert M. Speer, Acting Secretary of the Army, submitted by Ms. Schakowsky 133
Letter of May 10. 2017, from John Bel Edwards, Governor, State of Louisiana, to Robert M. Speer, Acting Secretary of the Army, submitted by Ms. Schakowsky 136
Letter of May 22, 2017, from Adam Gluck, Vice President and Head, U.S. Government Relations, Sanofi, to Mr. Murphy and Ms. DeGette, submitted by Ms. DeGette 138
Article of May 2017, "Emerging Infectious Diseases in Pregnancy," by Richard H. Beigi, Obstetrics & Gynecology, Vol. 129, No. 5, submitted by Mr. Burgess 140

U.S. PUBLIC HEALTH RESPONSE TO THE ZIKA VIRUS: CONTINUING CHALLENGES

TUESDAY, MAY 23, 2017

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 10:04 a.m., in Room 2123, Rayburn House Office Building, Hon. Tim Murphy (chairman of the subcommittee) presiding.

Members present: Representatives Murphy, Griffith, Burgess, Brooks, Collins, Barton, Walberg, Walters, Costello, Carter, Walden (ex officio), DeGette, Schakowsky, Castor, Tonko, Clarke, Ruiz, and Pallone (ex officio).

Also present: Mr. Bilirakis.

Staff present: Jennifer Barblan, Chief Counsel, Oversight and Investigations; Ray Baum, Staff Director; Elena Brennan, Legislative Clerk, Oversight and Investigations; Adam Fromm, Director of Outreach and Coalitions; Brittany Havens, Professional Staff Member, Oversight and Investigations; Katie McKeough, Press Assistant; David Schaub, Detailee, Oversight and Investigations; Jennifer Sherman, Press Secretary; Alan Slobodin, Chief Investigative Counsel, Oversight and Investigations; Sam Spector, Policy Coordinator, Oversight and Investigations; Evan Viau, Staff Assistant; Hamlin Wade, Special Advisor for External Affairs; Jeff Carroll, Minority Staff Director; Waverly Gordon, Minority Counsel, Health; Chris Knauer, Minority Oversight Staff Director; Miles Lichtman, Minority Policy Analyst; Kevin McAloon, Minority Professional Staff Member; Dino Papanastasiou, Minority GAO Detailee; Olivia Pham, Minority Health Fellow; and C.J. Young, Minority Press Secretary.

OPENING STATEMENT OF HON. TIM MURPHY, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF PENNSYLVANIA

Mr. MURPHY. Good morning, and welcome to our Oversight and Investigations Subcommittee hearing on "U.S. Public Health Response to the Zika Virus: Continuing Challenges."

Today, the subcommittee continues its examination of the Zika virus, and the subcommittee first examined the virus last year during the early stages of the outbreak across Central and South America.

As this year's mosquito season is about to begin, the time has come to review what has been done and what we have learned

since then and to examine the challenges that our Federal health agencies continue to face. To date, every State in the continental United States, minus Alaska, has reported cases of the Zika virus, and two States, Florida and Texas, have reported cases of locally acquired mosquito-borne transmission.

As of March 2017, there were 84 countries, territories, or subnational areas with evidence of vector-borne Zika virus, and 13 countries have reported evidence of person-to-person transmission of the virus.

A recent report released by the Centers for Disease Control and Prevention, or the CDC, found that 1 in 10 women in the United States with a confirmed Zika virus infection during pregnancy had a baby with a virus-related birth defect.

Emerging infectious diseases present unique challenges to public health systems here and around the world. When the committee held its hearing on Zika last March, much was unknown about the virus and its impact on public health. I want to commend our public health agencies for the work that they have all done. Diagnostic tools were quickly developed and approved under Emergency Use Authority, and more are in the pipeline now. Multiple vaccine candidates are in development, and much research into the virus and its effects have taken place. When instances of local transmission occurred in Florida and Texas, the CDC acted quickly in tandem with State and local partners to contain the spread.

But despite these efforts, the unknowns of this disease still outnumber the knowns. We don't know the actual number of infections in the United States. We don't know the long-term impact of Zika infection during pregnancy on children born to infected mothers. We don't know about the long-term impacts of infection on men or on people who exhibit no symptoms of Zika. There are difficulties with the diagnostic tests we have in use today, and we don't have good information or modeling on how the virus will spread this year, let alone beyond that.

The GAO is here today reporting on its evaluation of the U.S. public response to Zika, work commissioned by this committee. This is not the first time GAO has done such an analysis and response to emerging infectious diseases, and each time, GAO has found that HHS was reactive in its response to outbreak prevention, preparedness, detection, and response. Once again, GAO has shown that we are not fully prepared at the outset of the outbreak.

The GAO evaluated the U.S. public health response to Zika in three key areas: one, case definition and an understanding of how the disease spreads into community and the factors that affect this distribution; two, the development and use of diagnostic tools; and, three, methods of mosquito control.

The GAO findings are sobering. While there have been many advances, actions are needed to address major challenges. According to the GAO, the lack of standardized Zika case definition at the beginning of the outbreak complicated the collection of consistent and timely data. The diagnostic tests varied in their ability to detect the virus and provide accurate results. Manufacturers of diagnostic tests faced multiple challenges, including gaining access to FDA-authorized tests for comparison use, and the users of the tests

could not even determine the most accurate diagnostic tests based on the information provided.

And of great concern, the GAO report raises questions about CDC's and FDA's disclosure of test information and the treatment of CDC's own subject-matter expert, who was removed and then reinstated to his position after dissenting over concerns about the CDC Zika diagnostic tests provided to labs.

With regard to State and local mosquito control efforts, CDC developed technical guidance and provided funding and technical assistance. GAO identified challenges here as well for Federal agencies, including the need to effectively communicate information about the geographical distribution of the mosquito that primarily transmits the Zika virus. Much of the money appropriated by Congress last year to respond to Zika went to States and localities in the form of grants, and effective communication is critical to ensure that our Federal tax dollars are spent wising.

It is clear that we have much to discuss today. We will hear from a panel of distinguished Federal witnesses, including the Centers for Disease Control and Prevention, the National Institutes of Health, the Food and Drug Administration, the Biomedical Advanced Research and Development Authority, as well as the Government Accountability Office.

I want to thank all of our witnesses for joining us this morning.

[The prepared statement of Mr. Murphy follows:]

PREPARED STATEMENT OF HON. TIM MURPHY

Today the subcommittee continues its examination of the U.S. public health response to the Zika virus. The subcommittee first examined the Zika virus last year during the early stages of the outbreak across Central and South America. As this year's mosquito season is about to begin, the time has come to review what has been done-and what we have learned-since then, and to examine the challenges that our Federal health agencies continue to face.

To date, every State in the continental United States, minus Alaska, has reported cases of the Zika virus, and two States—Florida and Texas—have reported cases of locally acquired mosquito-borne transmission. As of March 2017, there were 84 countries, territories, or subnational areas with evidence of vector-borne Zika virus and 13 countries have reported evidence of person-to-person transmission of the virus. A recent report released by the Centers for Disease Control and Prevention (CDC) found that one in ten women in the United States with a confirmed Zika virus infection during a pregnancy had a baby with a virus-related birth defect.

Emerging infectious diseases present unique challenges to public health systems here and around the world. When the committee held its hearing on Zika in March of last year, much was unknown about the virus and its impact on public health. I want to commend our public health agencies for the work they have done. Diagnostic tools were quickly developed and approved under Emergency Use Authority, and more are in the pipeline now. Multiple vaccine candidates are in development, and much research into the virus and its effects have taken place. When instances of local transmission occurred in Florida and Texas, the CDC acted quickly in tandem with State and local partners to contain the spread.

But despite these efforts, the unknowns of this disease still outnumber the knowns. We don't know the actual number of infections in the United States. We don't know the long-term impact of Zika infection during pregnancy on children born to infected mothers. We don't know about the long-term impacts of infection on men, or on people who exhibit no symptoms of Zika. There are difficulties with the diagnostic tests we have in use today. And we don't have good information or modeling on how the virus will spread this year, let alone beyond that.

The GAO is here today reporting on its evaluation of the U.S. public health response to Zika-work commissioned by this committee. This is not the first time GAO has done such an analysis in response to emerging infectious diseases. And each time, GAO has found that HHS was reactive in its response to outbreak prevention,

preparedness, detection, and response. Once again, GAO has shown that we were not fully prepared at the outset of the outbreak.

The GAO evaluated the U.S. public health response to Zika in three key areas: (1) case-definition and an understanding of how the disease spreads into community and the factors that affect this distribution; (2) the development and use of diagnostic tools; and (3) methods of mosquito control. The GAO findings are sobering: while there have been many advances, actions are needed to address major challenges.

According to the GAO, the lack of a standardized Zika case definition at the beginning of the outbreak complicated the collection of consistent and timely data. The diagnostic tests varied in their ability to detect the virus and provide accurate test results. Manufacturers of diagnostic tests faced multiple challenges including gaining access to FDA-authorized tests for comparison use, and users of the tests could not even determine the most accurate diagnostic test based on the information provided.

And, of great concern, the GAO report raises questions about CDC's and FDA's disclosure of test information and the treatment of CDC's own subject matter expert who was removed and then reinstated to his position after dissenting over concerns about the CDC Zika diagnostic test being provided to labs.

With regard to State and local mosquito control efforts, CDC developed technical guidance and provided funding and technical assistance. GAO identified challenges here as well for Federal agencies, including the need to effectively communicate information about the geographical distribution of the mosquito that primarily transmits the Zika virus. Much of the money appropriated by Congress last year to respond to Zika went to States and localities in the form of grants, and effective communication is critical to ensure that our Federal tax dollars are spent wisely.

It is clear that we have much to discuss today. We will hear from a panel of distinguished Federal witnesses, including the Centers of Disease Control and Prevention, the National Institutes of Health, the Food and Drug Administration, the Biomedical Advanced Research and Development Authority, as well as the Government Accountability Office.

I would like to thank all of our witnesses for joining us this morning. I now recognize the ranking member of the subcommittee, Ms. DeGette, for a 5-minute opening statement.

Mr. MURPHY. I now recognize the ranking member of this subcommittee, Ms. DeGette, for a 5-minute opening statement.

OPENING STATEMENT OF HON. DIANA DEGETTE, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF COLORADO

Ms. DEGETTE. Thank you very much, Mr. Chairman.

This committee has been examining issues related to disease preparedness for more than a decade. We have looked recently at preparedness and response capabilities related to Ebola, seasonal flu, and pandemic flu, and, of course, now the Zika virus.

As you mentioned, last year, the Zika epidemic spread across Brazil, Latin America, and into the U.S. There were more than 5,000 Zika cases in the U.S. and over 36,000 in the U.S. territories.

Now, as we continue to face challenges with these epidemics and global pandemics, we can't be satisfied with simply reacting to each new emergency. Instead, we have to devote efforts and resources to ensuring that we're prepared before the next threat occurs. Oftentimes, we don't even know where those will come from.

We need to do more at the Federal and State levels to combat emerging infectious diseases. As I pointed out over a year ago, the bipartisan Blue Ribbon Study Panel on Biodefense concluded that the U.S. is underprepared for bioincidents, whether they're deliberate attacks or naturally occurring events. This is still a problem, despite our assiduous attention to it. For example, just this month, members of this subcommittee released a comprehensive GAO re-

port on avian flu. That audit uncovered shortcomings in our preparedness and raised key questions about our ability to rapidly respond to future outbreaks. GAO found that, while we can impose biosecurity measures after an emergency hits, our preparation is limited to voluntary actions, which are too often ineffective.

Today, we're going to hear again from the GAO, but this time on how our disease-fighting agencies are addressing the ongoing Zika threat and the remaining challenges. So, even though we're working on getting there, we're still not where we need to be when it comes to disease preparedness and emerging infectious threats.

I'm looking forward to hearing from all of the witnesses today about how we can improve processes in response to the GAO's recommendation.

I want to talk about another area, which is funding, and I know with the release of the President's budget today, everybody is concerned about funding. I'm really concerned about whether agencies have adequate funding to prepare and respond to a potential outbreak. We're fortunate to have premier public health agencies overseeing these efforts, but if their hands are tied with funding, those agencies can't do their work.

Last year, Congress made available $1.1 billion to fight Zika, but key agencies received far less money than they requested. In the end, agencies like the CDC had to reprogram funds to respond to this unfolding threat, diverting the funding from other top priorities.

This year, as I said, President Trump has proposed slashing HHS' budget and making deep cuts to public health agencies like the CDC or the NIH. This is so counterproductive. Now is not the time to make draconian threats—cuts to the agencies charged with stopping Zika or any other health crisis. Although we don't know what funds the administration will need to address the Zika threat for 2017, I don't have any reason to believe that they're going to need less than last year.

So I intend to ask the panelists whether they think that we're adequately resourced to go into the 2017 mosquito season. We don't want to find ourselves in the middle of this summer scrambling to cobble together another emergency supplemental.

And, finally, I want to welcome Dr. Petersen from Fort Collins here today. Dr. Petersen is the Director of the Division of Vector-borne Diseases, and that agency is in Fort Collins, Colorado. I went up and visited the facilities, Mr. Chairman, last year, and thanks to the efforts of former Congressman Bob Schaffer and myself, we were able to get new state-of-the-art facilities up there a few years ago. They're doing remarkable research, and I just want to thank you for adding your intelligence and your perspective today. And I also want to welcome all of our witnesses, of course.

And, with that, Mr. Chairman, I will yield back.

Mr. MURPHY. Thank you.

The gentlelady yields back, and I will recognize the chairman of the full committee for a 5-minute opening statement.

OPENING STATEMENT OF HON. GREG WALDEN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF OREGON

Mr. WALDEN. I thank the chairman.

Thank you for holding this timely hearing on U.S. public health response to the Zika virus. I want thank all of our witnesses for being here today and for providing us with your testimony.

For well over a year, our bipartisan committee staff have been working diligently to examine our public health preparedness for Zika and other emerging infectious diseases. This is our second hearing since the outbreak of this virus.

First, I want to commend the agencies that are appearing before us today. Each agency has undertaken a huge effort to increase our knowledge of the virus, to develop diagnostic tests and vaccine candidates quickly, and to educate our communities about how to respond to this virus and the mosquito that carries it.

I also want to commend the State and local entities that are working hard to treat those impacted by Zika and to reduce the population of Zika-carrying mosquitoes. While much progress has been made over the past year, the GAO released a report today showing our understanding and preparedness to combat this virus and other biological threats still face significant challenges. Particularly as we head into the summer months, we must do better.

Though the FDA has authorized two different types of diagnostic tests under the Emergency Use Authorizations, there's still no commercially available diagnostic tests on the market for the detection of the Zika virus. Currently, there are no specific therapies or vaccines approved by the FDA to prevent or treat the virus. Perhaps most concerning is we still don't know the full spectrum of health consequences associated with mother-to-child transmission, nor do we know what the short-term and long-term outcomes are for those who contract the virus with or without clinical symptoms.

We also continue to face significant issues in supporting mosquito control efforts and our ability to accurately model and predict the spread of viruses geographically. The number and implication of unknowns is frankly a bit alarming. It begs the question, how prepared are we for the next outbreak? Zika is not the only biological threat that we face today. As our society becomes increasingly global and world travel becomes easier, more efficient, and more frequent, the risk of spreading disease through human contact will increase rapidly.

Sadly, emerging infectious diseases, including Zika, Ebola, yellow fever, dengue, pandemic influenza, and others, perhaps many more that have yet to even be discovered threaten our human and bioterrorism defenses every day. The slides made famous on national television by our witness, Dr. Anthony Fauci, dramatizes the change from 30 years ago with just HIV as a global example of emerging infectious disease to a recent slide showing more than 40 examples.

Last year, the subcommittee held a hearing on the report of the Blue Ribbon Study Panel on Biodefense. It presented several concerns and expert recommendations to improve U.S. biodefense. The experts on the panel made it quite clear we need to stop thinking of disease preparedness and response as occasional episodic events, a reactive approach that's left us constantly lagging in our response efforts. Instead, we must shift our mindsets and strategies toward a broader, more comprehensive, and proactive approach, one that considers the larger context of our preparedness for future infectious diseases and outbreaks.

Federal witnesses testifying before us this morning are uniquely positioned to help aid in our efforts, and I thank you all for appearing before the subcommittee.

[The prepared statement of Mr. Walden follows:]

PREPARED STATEMENT OF HON. GREG WALDEN

Mr. Chairman, thank you for holding this very timely hearing on the U.S. public health response to the Zika virus.

For well over a year our bipartisan committee staff has been working diligently to examine our public health preparedness for Zika and other emerging infectious diseases. This is our second hearing since the outbreak of the virus.

First, I want to commend the agencies that are appearing before us today. Each agency has undertaken a huge effort to increase our knowledge of the virus, to develop diagnostic tests and vaccine candidates quickly, and to educate our communities about how to respond to this virus and the mosquito that carries it. I also want to commend the State and local entities that are working hard to treat those impacted by Zika, and to reduce the population of Zika-carrying mosquitoes.

While much progress has been made over the past year, the GAO report released today shows our understanding and preparedness to combat this virus—and other biological threats—still faces significant challenges. Particularly as we head into the summer months, we must do better.

Though the FDA has authorized two different types of diagnostic tests under Emergency Use Authorizations, there are still no commercially available diagnostic tests on the market for the detection of the Zika virus. Currently, there are no specific therapies or vaccines approved by the FDA to prevent or treat the virus.

Perhaps most concerning is that we still don't know the full spectrum of health consequences associated with mother-to-child transmission. Nor do we know what the short-term and long-term outcomes are for those who contract the virus, with or without clinical symptoms. We also continue to face significant issues in supporting mosquito control efforts and our ability to accurately model and predict the spread of viruses geographically.

The number and implication of unknowns is alarming. It begs the question: How prepared are we for the next outbreak?

Zika isn't the only biological threat that we face today. As our society becomes increasingly global and world travel becomes easier, more efficient, and more frequent, the risk of spreading disease through human contact will increase rapidly. Sadly, emerging infectious diseases including Zika, Ebola, yellow fever, Dengue, Chikungunya, pandemic influenza—and perhaps many more that have yet to be discovered—threaten our human and bioterrorism defenses every day. The slides made famous on national television by one of our witnesses, Dr. Anthony Fauci, dramatizes the change from 30 years ago with just HIV as the global example of emerging infectious disease to a recent slide showing more than 40 examples.

Last year, this subcommittee held a hearing on the report of the Blue Ribbon Study Panel on Biodefense, which presented several concerns and expert recommendations to improve U.S. biodefense. The experts on the panel made it quite clear that we need to stop thinking of disease preparedness and response as occasional, episodic events—a reactive approach that has left us constantly lagging in our response efforts. Instead, we must shift our mindsets and strategies towards a broader, more comprehensive, and proactive approach—one that considers the larger context of our preparedness for future infectious diseases and outbreaks.

The Federal witnesses testifying before us this morning are uniquely positioned to help aide us in these efforts, and I thank them for appearing before the subcommittee this morning.

Mr. WALDEN. And I yield the balance of my time to the chairman of the Health Subcommittee, Dr. Burgess.

Mr. BURGESS. Thank you, Mr. Chairman. Thank you for yielding.

So, to paraphrase the Rolling Stones, summer is here, and the time is right for fighting vectors in the street. I want to thank our panelists for being here today. Some new faces, and that will be good to get to know you a little bit better, and some people that we have talked with many times before.

And, Dr. Fauci, just thinking back to the 108th Congress, we talked about SARS, we talked about avian flu, we talked about swine flu, we talked about Ebola, and we talked about Zika. And every one of those illnesses, of course, has a particular impact upon women and pregnancy, and that has certainly been—and I appreciate the focus that you have put on that during the times that we have had the privilege of having you before our subcommittee.

So I want to welcome our witnesses. Look forward to what your testimony is going to be today.

And, Mr. Chairman, I yield back.

Mr. MURPHY. With that then——

Ms. DEGETTE. Will the gentleman yield? It is not the Rolling Stones. It is Bruce Springsteen.

Mr. MURPHY. The record will stand corrected.

Mr. BURGESS. No, no, no correction of the record. I will put my iTunes against yours.

Mr. MURPHY. Thank you. Well, we reached a new level for this hearing. The gentleman yields back.

I recognize Mr. Pallone for 5 minutes.

Mr. PALLONE. I won't comment because I don't know.

OPENING STATEMENT OF HON. FRANK PALLONE, JR., A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Thank you, Mr. Chairman, and thank you to all our witnesses for joining us this morning to discuss the Federal Government's preparations for the 2017 Zika season. I look forward to hearing from our panelists today about how they believe the Zika virus will spread in 2017, what they anticipate the upcoming mosquito season will look like, what challenges remain, and what additional resources they need to do their job.

In March of 2016, the committee held a hearing to examine the Federal Government's response to the spreading Zika threat. Since then, we have learned a great deal more about this virus. For example, scientific consensus now indicates that Zika infections in mothers during pregnancy can cause microcephaly in newborns, a severe birth defect of the brain.

As we'll hear from GAO today, although CDC and FDA took steps to respond to the unique challenges posed by the Zika outbreak last year, there remains room for improvement. This is particularly true regarding our ability to predict the spread of Zika, to better coordinate and control mosquito populations at the local level, and to more rapidly develop diagnostic tests for detecting Zika infection.

These steps to improve preparedness should also go hand-in-hand with strengthening our healthcare programs. We must ensure that individuals affected by Zika, particularly pregnant women and children born with microcephaly, have access to ongoing screening and health services.

An integral part of that effort is the Medicaid program. Medicaid provides contraceptive services that help prevent Zika infection and diagnostic services to detect infection. Medicaid is also a vital source of care for children born with special healthcare needs like microcephaly.

Today, Medicaid covers one in three children in the United States. The President's budget is expected within the hour, and there are reports that he plans to propose slashing Medicaid by over $800 billion, and this would decimate the Medicaid program and endanger our ability to manage public health emergencies like Zika.

I also remain concerned about the status of Medicaid funding in Puerto Rico. As everyone in this room understands, Zika has wreaked havoc upon Puerto Rico, yet as we head into the 2017 mosquito season, funding for Puerto Rico's Medicaid program through the Affordable Care Act is on track to be exhausted as early as this October. And despite the $295 million allocated for Medicaid funding in Puerto Rico as part of the recent continuing resolution, up to 900,000 people remain at risk of losing their health coverage at the end of this year.

So, in short, a strong public health infrastructure is also one of the best tools to fight epidemics, and Medicaid is an essential component in protecting us from threats such as Zika. Fighting Zika will not be easy, but the first step should be to maintain critical health services for those who may be affected and provide agencies with the resources they will need to respond to an outbreak.

Now I'm concerned about recent reports that nearly 700 positions at CDC are vacant because of the ongoing hiring freeze and that Federal support to States for Zika response may be discontinued. That's why Democratic members of this committee sent a letter to CDC last week asking whether the agency has sufficient funding to prepare and respond to Zika this year. It is critical that we give these agencies the tools they need to bolster our preparedness.

So let me conclude by saying thank you to the agencies before us today who work on a daily basis to fight this disease. I don't think anybody else wants to—you would like to? I yield the balance of my time to the gentlewoman from Florida.

[The prepared statement of Mr. Pallone follows:]

PREPARED STATEMENT OF HON. FRANK PALLONE, JR.

Thank you, Mr. Chairman, and thank you to all our witnesses for joining us this morning to discuss the Federal Government's preparations for the 2017 Zika season.

I look forward to hearing from our panelists today about how they believe the Zika virus will spread in 2017, what they anticipate the upcoming mosquito season will look like, what challenges remain, and what additional resources they need to do their job.

In March of 2016, this committee held a hearing to examine the Federal Government's response to the spreading Zika threat. Since then, we have learned a great deal more about this virus. For example, scientific consensus now indicates that Zika infection in mothers during pregnancy can cause microcephaly in newborns, a severe birth defect of the brain.

As we will hear from GAO today, although CDC and FDA took steps to respond to the unique challenges posed by the Zika outbreak last year, there remains room for improvement. This is particularly true regarding our ability to predict the spread of Zika, to better coordinate and control mosquito populations at the local level, and to more rapidly develop diagnostic tests for detecting Zika infection.

These steps to improve preparedness should also go hand-in-hand with strengthening our health care programs. We must ensure that individuals affected by Zika, particularly pregnant women and children born with microcephaly, have access to ongoing screening and health services.

An integral part of that effort is the Medicaid program. Medicaid provides contraceptive services to help prevent Zika infection, and diagnostic services to detect infection. Medicaid is also a vital source of care for children born with special health

care needs, like microcephaly. Today, Medicaid covers 1 in 3 children in the United States.

The President's budget is expected within the hour, and there are reports that he plans to propose slashing Medicaid by over $800 billion. This would decimate the Medicaid program and endanger our ability to manage public health emergencies like Zika.

I also remain concerned about the status of Medicaid funding in Puerto Rico. As everyone in this room understands, Zika has wreaked havoc upon Puerto Rico. Yet, as we head into the 2017 mosquito season, funding for Puerto Rico's Medicaid program through the Affordable Care Act is on track to be exhausted as early as this October.

And despite the $295 million allocated for Medicaid funding in Puerto Rico as part of the recent Continuing Resolution, up to 900,000 people remain at risk of losing their health coverage at the end of this year.

In short, a strong public health infrastructure is often one of the best tools to fight epidemics, and Medicaid is an essential component in protecting us from threats such as Zika. Fighting Zika will not be easy, but the first step should be to maintain critical health services for those who may be affected and provide agencies with the resources they will need to respond to an outbreak.

I'm concerned about recent reports that nearly 700 positions at CDC are vacant because of the ongoing hiring freeze, and that Federal support to States for Zika response may be discontinued. That is why Democratic members of this committee sent a letter to CDC last week asking whether the agency has sufficient funding to prepare and respond to Zika this year. It is critical that we give these agencies the tools they need to bolster our preparedness.

Let me conclude by saying thank you to the agencies before us today who work on a daily basis to fight this disease.

Thank you, and I yield back.

Ms. CASTOR. Thank you, Mr. Pallone, for yielding the time.

I'm very concerned for families all across American and particularly in the State of Florida and Puerto Rico because the birth defects related to the Zika virus are so severe and costly and because America's emergency public health response to Zika is at risk right now. After the Congress provided a billion dollars last year, we ramped up an emergency public health response that included our local communities, States, extensive surveillance, mosquito control, laboratories, development of vaccines, but as we stand now, there are too many unanswered questions about transmission of Zika and the medical consequences. Our families are at risk because of that.

They're also at risk because we're facing a funding cliff for the Zika emergency response. What is the most important in a public health emergency response is you have consistency. And right now, all of the agencies in local communities and States are looking at this cliff that's going to come to the end over the next few weeks, definitely by September.

I see great risk because of the hiring freeze that the Trump administration put into place that is now keeping public health professionals off the job at CDC and NIH and other important agencies. And then, with the budget that comes out today, we're going to have to deal with this overarching desire by the Trump administration to pull the rug out from under families because they're going to target cuts to medical research and the Centers for Disease Control all at the time where they say we're going to give big tax cuts to billionaires who will have all the resources in the world to deal with a Zika diagnosis in their family, but meanwhile, families across America will be left with very serious consequences.

So this committee needs to develop a plan of action in the coming weeks, and hopefully the expert advice from this panel will help guide us there. Thank you very much.

Mr. MURPHY. The gentlelady's time is expired.

At this point, I just want to say that I ask unanimous consent that the Members' written opening statements be introduced into the record and, without objection, the documents be entered into the record.

I now would like to introduce our panel of Federal witnesses for today's hearing: Dr. Timothy Persons, Chief Scientist, U.S. Government Accountability Office; Dr. Lyle Petersen, Director, Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention; Dr. Luciana Borio, Acting Chief Scientist, U.S. Food and Drug Administration; Dr. Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases, National Institutes of Health; and Dr. Rick Bright, Director of Biomedical Advanced Research and Development Authority and Deputy Assistant Secretary for Preparedness and Response, U.S. Department of Health and Human Services. Thank you all for being here today and providing testimony.

We look forward to a very productive discussion and how we can better prepare for and respond not only to Zika virus but to all the emerging infectious diseases and biological threats to our Nation.

You are aware this committee is holding an investigative hearing and, when doing so, has a practice of taking testimony under oath. Do any of you have any objections to giving testimony under oath?

Seeing none, the Chair then advises you that, under the rules of the House and the rules of the committee, you are entitled to be advised by counsel. Do any of you desire to be advised by counsel during testimony today?

No one has indicated that. Then, in that case, will you please rise, raise your right hand, and I will swear you in.

[Witnesses sworn.]

Mr. MURPHY. Thank you. You may all be seated.

Seeing that all have answered in the affirmative, you are now under oath and subject to the penalties set forth in title 18 under section 1001 of the United States Code. We'll ask you each to give a 5-minute summary of your written statement. Please pay attention to the light there.

Dr. Persons, you are recognized first for 5 minutes.

STATEMENTS OF TIMOTHY M. PERSONS, PH.D., CHIEF SCIENTIST, GOVERNMENT ACCOUNTABILITY OFFICE; LYLE R. PETERSEN, M.D., DIRECTOR, DIVISION OF VECTOR–BORNE DISEASES, NATIONAL CENTER FOR EMERGING AND ZOONOTIC INFECTIOUS DISEASES, CENTERS FOR DISEASE CONTROL AND PREVENTION; LUCIANA BORIO, M.D., ACTING CHIEF SCIENTIST, FOOD AND DRUG ADMINISTRATION; ANTHONY S. FAUCI, M.D., DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH; AND RICK A. BRIGHT, PH.D., DIRECTOR, BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY, AND DEPUTY ASSISTANT SECRETARY, OFFICE OF THE ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE, DEPARTMENT OF HEALTH AND HUMAN SERVICES

STATEMENT OF TIMOTHY M. PERSONS

Dr. PERSONS. Thank you, Mr. Chairman. Good morning and good morning, Ranking Member DeGette and members of the subcommittee. Thank you for the opportunity to discuss our work on the Federal response to Zika virus disease outbreaks with particular focus on epidemiology, diagnostic tests, and mosquito control. As this committee has pointed out even this morning, emerging infectious diseases, such as Zika virus disease, are an ongoing threat to the health and livelihoods of people and animals worldwide.

Despite many advances in medical research and treatments during the past century, infectious diseases are still a leading cause of death. Over the past few decades, several emerging infectious diseases have similarly taken the global community by surprise, including H1N1 influenza, Ebola, and Zika, among others.

In each case, the Department of Health and Human Services, though diligent in its work to address rapidly emerging threats, was nonetheless reactive in some respects, such as outbreak prevention, preparedness, detection, and response. Although HHS has key agencies working on various important aspects of this problem, currently no one person or agency is in charge of making sure the U.S. is ready for the next outbreak of an emerging infectious disease.

The Zika virus attracted attention from health officials here and abroad after causal links were suspected between increases in reported cases of Zika virus infection and reported cases of microcephaly in newborns and other neurological disorders in Brazil in 2015.

An effective response to an emerging infectious disease like Zika involves the establishment of a case definition, gaining an understanding of the disease's spread into the population, rapidly developing and deploying reliable diagnostic tools at the beginning of the outbreak, and, when the disease is vector-borne as Zika is, effective methods of mosquito control.

While recent Zika virus disease outbreaks have yielded new insights, several key unknowns remain, including the total number of infections, various biological mechanisms and risk factors, and

the full spectrum of short- and long-term outcomes of Zika virus infection, among others.

We also identify two key challenges for Zika virus epidemiological research. One is the time and resources needed to better understand the short- and long-term effects of Zika virus disease, and the other is an insufficiency of data and a lack of computer models for predicting the spread of Zika virus. Moreover, at the beginning of the U.S. outbreak, there was no U.S. medical case definition, despite there being candidates from other affected countries.

Even though the U.S. had known about and was conducting surveillance on Zika virus disease outbreaks, including those in U.S. territories, no accurate and reliable diagnostic tools had been authorized. The FDA had authorized over 15 diagnostic tests for the Zika virus under the Emergency Use Authorization process following the public health emergency declaration.

Manufacturers of diagnostic tests face several challenges, including lack of knowledge of key scientific aspects of the virus, difficulty in accessing well-characterized clinical samples, getting access to EUA samples to use for comparison, gaining cooperation with international entities, and according to some, a lack of effective communication from the FDA.

One major issue users face with these diagnostic tests is that it was not possible for them to easily compare the tests based on information on the product insert. Users of the tests also identified challenges that included, for example, complying with a test EUA label specifying certain equipment required to perform the test and determining the most accurate test, in part because of the challenges comparing performance characteristics reported in the EUA labels.

Turning to mosquito-control efforts, the Federal Government has a limited and indirect role in supporting them since they were implemented at the State and local levels. CDC developed technical guidance and provided funding and technical assistance to support State and local mosquito-control activities but does not serve, nor does any other agency serve, as a central coordinator for mosquito control nationwide.

We identify four challenges the Federal Government faced in supporting these mosquito-control efforts during the Zika virus outbreaks. One is the timing and availability of the funds, including the sustaining of expertise throughout the year. Second is the limited communication about the actual distribution of mosquitoes. Third is linking the effects of mosquito control to disease outcomes. And fourth is having limited information about mosquito-control entities themselves.

In short, our report indicates that there's still work to be done to better coordinate and more effectively implement mosquito control nationwide. In conclusion, HHS has led the way in making progress in our understanding of the Zika virus disease, but several challenges remain. Although the EUA process is aimed at getting the diagnostic tests out quickly in emergency situations, it is equally important to clinical users that the authorized tests be compared to one another with respect to key performance characteristics. That will allow them to determine which is the most appropriate.

We have identified several areas where improvements can be made and have made five recommendations. HHS agreed with four, partially concurred with the fifth, and provided clarifying information. In response to our recommendation to include information on CDC-developed tests distributed to public health laboratories, HHS agreed that it should share information on such tests that have received EUA. However, HHS did not agree with our recommendation that it should share information on CDC's lab-developed tests that have not received EUA because CDC is unable to provide detailed information on the characteristics of these unstandardized tests.

Mr. MURPHY. Dr. Persons, we are way over time. Do you have a final thought?

Dr. PERSONS. Yes, sir. We maintain that sharing information about the lab-developed tests that are used for comparison is important because it could help other diagnostic test users about which tests to adopt or recommend.

Chairman Murphy, Ranking Member DeGette, and members of the subcommittee, this concludes my prepared statement. Thank you for your sustained attention on this issue, and I would like to thank the GAO team who made this testimony possible. I'll be happy to answer your questions.

[The prepared statement of Dr. Persons follows:]

United States Government Accountability Office

GAO

Testimony
Before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, House of Representatives

For Release on Delivery
Expected at 10:00 a.m. ET
Tuesday, May 23, 2017

EMERGING INFECTIOUS DISEASES

Actions Needed to Ensure Improved Response to Zika Virus Disease Outbreaks

Statement of Timothy M. Persons, Ph.D., Chief Scientist

GAO Highlights

Highlights of GAO-17-612T, a testimony before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, House of Representatives.

Why GAO Did This Study

Zika virus disease can cause adverse health outcomes. This statement summarizes the findings of GAO's May 2017 report that is being released concurrently on progress made and challenges faced by federal agencies in responding to the Zika virus outbreak in the United States.

GAO examined (1) information on what is known and not known about the epidemiology of the Zika virus and challenges with conducting surveillance and epidemiological studies, (2) characteristics of different authorized diagnostic tests, challenges test manufacturers and users faced, and the extent to which FDA and CDC followed their own communication guidance, and (3) the strengths and limitations of available mosquito control methods, and challenges federal agencies faced.

GAO reviewed documents and interviewed officials about the Zika virus response. GAO also convened an expert meeting with the assistance of the National Academy of Sciences to discuss various issues related to Zika virus.

What GAO Recommends

In its May report GAO made five recommendations to FDA and CDC, including that CDC establish a transparent process for providing test manufacturers access to diagnostic tests for comparison purposes and FDA and CDC provide information to help ensure that users of diagnostic tests can compare performance. The agencies agreed with four recommendations and partially with the fifth and identified actions to implement them.

View GAO-17-612T. For more information, contact Chief Scientist Timothy M. Persons at (202) 512-6412 or personst@gao.gov.

May 23, 2017

EMERGING INFECTIOUS DISEASES

Actions Needed to Ensure Improved Response to Zika Virus Disease Outbreaks

What GAO Found

Since Zika virus disease was a newly emerging disease threat in the United States, the Centers for Disease Control and Prevention (CDC), and the states were not fully equipped with needed information and resources at the beginning of the outbreak. This presented several challenges for surveillance and research efforts, such as establishing a national definition for reporting cases. Knowledge about Zika virus epidemiology has increased in the past year, for example, its associated adverse health outcomes, and various modes of transmission. Most of the 5,197 Zika virus disease cases reported by April 5, 2017 across 49 states in the United States were associated with travel to affected areas outside the continental United States; only two states—Florida and Texas—reported local mosquito-borne transmission—216 were in Florida and 6 in Texas. The vast majority of the 36,504 cases reported in U.S. territories have been acquired through presumed local, mosquito-borne transmission in Puerto Rico. While much has been learned about the epidemiology of the Zika virus, many unknowns remain, including the actual number of infections in the United States and the full spectrum of short-term and long-term outcomes.

The 16 Zika virus diagnostic tests authorized during the outbreak varied in their performance and operational characteristics. For example, they varied in their ability to detect the virus and provide accurate results. In developing the diagnostic tests, manufacturers faced challenges in several areas, including access to clinical samples and other authorized diagnostic tests for comparison purposes. Users of the tests also encountered challenges, including determining the most accurate test to use, having access to different tests, and obtaining equipment needed to conduct the tests. Some manufacturers raised concerns about the difficulty in developing diagnostic tests that met the Food and Drug Administration's (FDA) requirements for Emergency Use Authorization and some users expressed concerns about selecting tests amongst those authorized. GAO also determined that CDC and FDA did not consistently communicate sufficient information about diagnostic tests, including providing clear information that would have enabled users to more easily compare performance across different tests.

Mosquito control programs in the United States are implemented at state and local levels and are critical to mitigating the risks associated with the Zika virus. Control methods include applying pesticides, reducing available water sources for breeding, and using personal protection. Each method has its strengths and limitations. For example, some control methods are more effective at reducing mosquito populations while others help prevent individuals from mosquito bites. Similarly, each method has some limitations, for example, there is varied public opposition to the use of certain pesticides. CDC supports state and local mosquito control activities primarily by providing guidance on mosquito control methods and funding to support certain mosquito control efforts. Challenges federal agencies identified in supporting these activities include sustaining staff expertise in mosquito control during periods when there are no outbreaks, funding constraints, and effectively communicating information about the geographical distribution of mosquitoes that transmit the Zika virus.

Chairman Murphy, Ranking Member DeGette, and Members of the Subcommittee:

Thank you for the opportunity to discuss our work on the federal response to Zika virus disease outbreaks, with particular focus on epidemiology, diagnostic tests, and mosquito control. Emerging infectious diseases, such as Zika virus disease, are an ongoing threat to the health and livelihoods of people and animals worldwide. Despite many advances in medical research and treatments during the past century, infectious diseases are still a leading cause of death worldwide. Our testimony today summarizes our report entitled *Emerging Infectious Diseases: Actions Needed to Address the Challenges of Responding to Zika Virus Disease Outbreaks* which is being released today.[1] We have also issued several other reports on infectious diseases.[2]

Zika virus disease is caused by the Zika virus, which is spread to people primarily through the bite of an infected mosquito (*Aedes aegypti*). Many people with Zika virus infection will not have any signs or symptoms or will have only mild symptoms. The Zika virus attracted attention from health officials in the United States and abroad after associations were suspected between increases in reported cases of Zika virus infection and reported cases of microcephaly in newborns and other neurological syndromes in Brazil in 2015.[3]

Several U.S. federal agencies are involved in the response to Zika virus disease outbreaks. Specifically, the Centers for Disease Control and Prevention (CDC) collects data from states on reported cases of nationally notifiable diseases through surveillance systems. The Food and Drug Administration (FDA) oversees the safety and effectiveness of diagnostic tests. The Secretary of Health and Human Services (HHS) can make a declaration of emergency that can allow FDA to issue Emergency Use Authorization (EUA) of medical products to be used when adequate, approved, and available alternatives are lacking. FDA's website includes

[1]GAO, *Emerging Infectious Diseases: Actions Needed to Address the Challenges of Responding to Zika Virus Disease Outbreak*, GAO-17-445 (Washington, D.C.: May 23, 2017).

[2]For a full list of related reports please see GAO-17-445.

[3]Microcephaly is a rare nervous system disorder that causes a baby's head to be smaller than expected and not fully developed, which can lead to impaired thought processes, delayed motor function, and other adverse outcomes.

a current list of available diagnostic tests and associated information about each test. FDA has authorized two different types of diagnostic tests for the Zika virus—molecular and serologic.[4]

Our May 2017 report and my statement today address (1) what is known and not known about the epidemiology of the Zika virus, and challenges in conducting surveillance and epidemiological studies, (2) characteristics of different Zika virus authorized diagnostic tests, challenges manufacturers and users of diagnostic tests have faced, and the extent to which CDC and FDA followed their own communication guidance concerning diagnostic tests during the recent U.S. outbreak, and (3) available mosquito control methods, their strengths and weaknesses, and challenges federal agencies face in assisting mosquito control efforts.[5]

For our May 2017 report, we reviewed agency documents including reports on Zika virus epidemiology, diagnostic testing guidance, agency documents on mosquito control, and information on all authorized diagnostic tests for Zika virus disease. We also interviewed the manufacturers of authorized tests, officials from key federal agencies and departments, selected state and local public health entities, and public health organizations responding to the domestic Zika virus outbreak. We also convened, with the assistance of the National Academy of Sciences, a meeting with 16 experts from federal and state governments, academia, and industry who combined knowledge of Zika virus epidemiology, diagnostic testing, and mosquito control, to identify and discuss experiences and challenges that arose during the Zika virus outbreak response. Additional information on our scope and methodology is available in our report. We performed the work on which this testimony is based in accordance with generally accepted government auditing standards.

[4]Molecular tests are used to detect genetic material in samples of bodily fluids such as serum and urine. Serologic tests are diagnostic tests that detect antibodies against the Zika virus.

[5]For the purpose of the report and this testimony, users of diagnostic tests include laboratory personnel, health care providers, and others in the medical and scientific communities.

Challenges to Gathering New Information about Zika Virus Epidemiology

Surveillance and research conducted during the recent Zika virus disease outbreaks around the world have established some new knowledge about the epidemiology of the Zika virus, including information about the incidence of the disease and the distribution of cases, and its associated adverse health outcomes. Most of the 5,197 Zika virus disease cases reported by April 5, 2017 across 49 states in the United States were associated with travel to affected areas outside the continental United States; only two states—Florida and Texas—reported local mosquito-borne transmission—216 were in Florida and 6 in Texas. Most of the 36,504 cases reported in U.S. territories have been acquired through presumed local, mosquito-borne transmission in Puerto Rico. According to the World Health Organization (WHO) and CDC, there is now evidence that the Zika virus causes microcephaly, brain abnormalities, and other birth defects and neurological disorders, based on the totality of evidence from current epidemiological and clinical studies.

Nevertheless, many unknowns about the Zika virus remain, including (1) the total number of people with symptomatic and asymptomatic infections, (2) the biological mechanisms, risks, reasons for geographic differences, and the full spectrum of outcomes associated with maternal-fetal transmission, (3) the presence and duration of the virus in different bodily fluids, and (4) the role of prior exposure to Zika and other closely related viruses in risk and severity of Zika virus disease outbreaks, and (5) the full spectrum of outcomes associated with Zika virus infection.

When the outbreak started in the United States, CDC, and state and local public health agencies, and public health organizations, faced some challenges in establishing and implementing surveillance systems for Zika virus disease and infection and its associated health outcomes. Challenges included establishing surveillance case definitions early in the outbreak when little was known about the Zika virus, timely communication of critical information that was rapidly evolving, and the lack of interoperability between surveillance systems. We also identified two key challenges for epidemiological research: (1) time and resources required for studies needed to establish association and causality between the Zika virus and associated health outcomes and (2) insufficient data and models for predicting the spread of the Zika virus.

Characteristics of Different Diagnostic Tests Varied, Manufacturers and Users Faced Several Challenges, and FDA and CDC Did Not Consistently Communicate Sufficient Information

By April 12, 2017, FDA had authorized 16 diagnostic tests for the Zika virus under EUAs, following a public health emergency declaration.[6] In response to the Zika virus outbreak, CDC manufactured and received EUA from FDA for both molecular and serologic tests. We found that authorized diagnostic tests used for the recent Zika virus outbreak varied in their performance and operational characteristics. Molecular and serologic tests have different strengths and limitations, but some of the limitations can be mitigated by using the CDC algorithm.

It is important to recognize that a negative molecular test does not rule out Zika virus infection because the amount of virus in the sample could be too low to be detected at the time of molecular testing. Some scientists expressed concern over the limit of detection for the Zika virus by some authorized molecular diagnostic tests, which could have resulted in molecular testing missing Zika infections. CDC provided guidance intended to reduce the risk of inaccurate results by recommending that molecular tests should be further tested with a serological test. One critical issue with serological Zika virus disease testing is potential cross-reactivity – when antibodies to similar viruses react. For example, cross-reactions occur in the diagnostic tests for Zika and dengue because these viruses are closely related.

We identified challenges that manufacturers of diagnostic tests for Zika virus faced including: (1) lack of knowledge of biological aspects of the virus and immune response, (2) difficulty in accessing well-characterized clinical samples, (3) getting access to EUA tests for use as a comparator test, and (4) gaining cooperation with international entities.[7]

The first challenge manufacturers faced was uncertainty at the beginning of the outbreak about which sample type to use for molecular testing. For instance, the Zika virus had been found to be present longer in urine than in blood, but information on how long the virus could persist in different bodily fluids was still evolving making it difficult to develop diagnostic tests.

[6]FDA authorized 13 molecular tests and 3 serologic tests. According to FDA officials, they revoked one test, and as a result, 15 diagnostic tests are currently authorized.

[7]FDA recommends that manufacturers perform clinical evaluation studies that compare their tests to another "comparator" assay that is laboratory developed, an in-house test, or an EUA test.

Second, during the early stages of the outbreak there was a lack of well-characterized clinical samples for Zika virus diagnostic test development. Several manufacturers told us that there were insufficient quantities of available samples, and samples that were available were expensive.

Third, FDA recommends that manufacturers perform clinical evaluation studies that compare their new tests to another "comparator" assay (test).[8] Similarly, a CDC document states that CDC should provide a consistent, fair, and transparent review process for all public-private initiatives, even during emergencies. According to CDC officials, the CDC developed EUA tests were not made available to some commercial manufacturers for use as comparator tests because these tests are distributed only to public health laboratories performing Zika virus clinical diagnoses. Moreover, according to CDC officials, in the early stage of the response CDC did not have the capacity to both adequately support public health laboratories and also supply commercial manufacturers with these tests. Ultimately, CDC distributed its tests to four manufacturers through technology transfers and we found that 2 of the 12 authorized molecular diagnostic test labels listed CDC's test as their comparator test. However, one manufacturer told us their request to CDC for reagents to perform the CDC test as a comparator test was denied because they were a commercial manufacturer. CDC officials we spoke with were unclear of how the process to transfer authorized CDC tests to manufacturers originally started. *Standards for Internal Control in the Federal Government* state that agencies should document their operational processes to ensure that the organization meets its objectives.[9] Without a clear and transparent process for distributing CDC diagnostic tests, CDC may not be able to support the development of capacity in the commercial sector to meet the needs during an outbreak.

Fourth, interacting with international entities to obtain samples and perform testing presented challenges for manufacturers. For instance, foreign countries have different laws that must be followed. A manufacturer we interviewed tried to bring equipment to perform a diagnostic test into another country for testing but it faced challenges getting the necessary import license.

[8]CDC was the first manufacturer to receive an EUA, and therefore the CDC test was the first authorized molecular test to which other manufacturers attempting to get EUA could compare their tests.

[9]GAO, *Standards for Internal Control in the Federal Government*, GAO-14-704G (Washington, D.C.: September 2014).

We also found that some diagnostic test users faced challenges complying with equipment requirements to perform tests as specified in the EUA labels, and determining the most accurate test. Moreover, although CDC officials told us that all states had at least one public health laboratory that had the equipment to run a CDC test, representatives from several laboratories we interviewed told us they had to acquire specific new specialized equipment to be able to perform a certain EUA diagnostic test.

An FDA document states that the agency should share information that is up-to-date, understandable, and easily accessible so diagnostic test users have some basis for choosing which medical products to purchase and use. We found that although performance characteristics are listed on individual diagnostic test labels, they are not available in a consolidated format. According to FDA officials, the agency began collecting information using reference samples because different manufacturers were using different types of samples and potentially different methods to determine the limit of detection of their tests. Until limit of detection data have been extracted and summarized from all the diagnostic test labels, it may be difficult and time-consuming for users to compare the performance characteristics and results of diagnostic tests.

Another challenge users faced was that without knowing the identity of the comparator test, it was more difficult for them to compare performance characteristics across different diagnostic tests and determine the most appropriate test for them to use. Experts at our meeting agreed that identifying the comparator test would make it easier to compare the risks and benefits of different Zika virus diagnostic tests. An FDA document recommends a clear description of all methods used and how and what data were collected when performing comparison testing, including a description of the comparator test. When we compared product labels for different molecular tests, we found that while labels listed the type of test used for comparison, 6 of 12 product labels did not list the identity of the test used for comparison. FDA officials stated that the comparator test for authorized diagnostic tests can either be another authorized test or a validated reference method, and that manufacturers are not required to identify the comparator test used. FDA staff told us they are concerned that labels identifying comparator tests could be used to make inappropriate claims or be misinterpreted by end users.

Standards for Internal Control in the Federal Government state that agencies are to communicate quality information externally through

reporting lines so that external parties can help an entity achieve its objectives and address related risks. CDC did not make publically available data comparing the performance characteristics of different CDC diagnostic tests that it distributed during the outbreak. CDC's website has information about the performance of its two authorized diagnostic tests but not the laboratory developed test it distributed. According to a HHS report, CDC did not provide information about one of its diagnostic tests because it could potentially create confusion and could have caused public health laboratories to discontinue use of an EUA test, and it had not done a comprehensive comparison of the two tests. Because CDC did not publicly provide performance information about its laboratory developed test—which was distributed to some public health laboratories—questions arose regarding the sensitivity of the two CDC tests.

Representatives of three scientific professional societies told us that information about the development and verification of CDC's diagnostic tests should be made available to the scientific and medical communities. Access to such data would provide transparency and allow for optimal patient care, according to these representatives. According to these scientific professional societies' representatives, the lack of access to data regarding test performance prevented laboratory professionals from making informed decisions about which test to adopt or recommend during the outbreak. Without including information on the performance characteristics of tests it is distributing, CDC cannot ensure that healthcare providers and the public have the information they need to make informed decisions about which test is best for their use.

In our May 2017 report we recommend that FDA consolidate information from individual diagnostic test labels and make it available in a form that enables diagnostic test users to more readily compare information across tests and require manufacturers of diagnostic tests to list the identity of comparator tests on their labels. We also recommend that CDC establish a transparent process to provide CDC diagnostic tests, on request, to manufacturers that are in the final stages of diagnostic test authorization, and include information on CDC-developed tests, including laboratory developed tests. HHS agreed with our recommendations for FDA to consolidate information about tests, require manufacturers to list the identity of the comparator assay, and that CDC establish a transparent process for distributing CDC-developed tests. In response to our recommendation to include information on CDC-developed tests distributed to public health laboratories, HHS partially concurred and provided clarifying information. HHS agreed that it should share

information on CDC-developed tests that have received EUA. However, regarding this recommendation, HHS did not agree with our recommendation that it should share information on CDC's laboratory-developed tests that have not received EUA because CDC is unable to provide detailed information on characteristics of these unstandardized tests. We maintain that sharing information about these laboratory developed tests that are used for comparison testing is important because of the concerns that were raised regarding the sensitivity of one of CDC's EUA tests. We recognize that laboratory-developed tests that have not received EUA are not standardized, but we believe that CDC can provide certain information on the performance characteristics and quality of these tests based on its knowledge about these tests. Sharing this information could help other diagnostic test users make informed decisions about which test to adopt or recommend. HHS also noted that CDC does not distribute laboratory developed tests that have not received EUA but shares them with public health laboratories. In response to this comment, we modified our recommendation to reflect this information.

Mosquito Control Methods Have Strengths and Limitations, and Federal Agencies Are Challenged in Assisting These Efforts

Different types of mosquito control methods are available in the United States and each has strengths and limitations. The methods can be combined with surveillance of the mosquito population, using an integrated approach (i.e., pesticide use, traps, public education programs, and others) to optimize the application of multiple control methods, depending on knowledge of mosquito biology and distribution.

Because Zika virus disease is not yet preventable by known drugs or vaccines, mosquito control is critical in mitigating risks associated with this disease. Mosquito control in the United States is implemented and overseen by state and local entities such as mosquito control districts and health agencies. CDC, through sources including the American Mosquito Control Association, identified over 900 entities in the United States that perform mosquito control; however, not all geographic areas in the United States are covered. Federal agencies may support such control entities with funding, subject matter expertise, and may regulate some control methods such as pesticides.

The federal government has a limited and indirect role in supporting mosquito control efforts, which are mainly implemented at the state and local levels. According to CDC documentation, the agency developed technical guidance and provided funding and technical assistance to support state and local mosquito control activities. We identified four challenges the federal government faced in supporting these mosquito

control efforts during the Zika virus outbreaks: (1) timing of the availability of resources and sustaining expertise, (2) communicating information about current mosquito distribution, (3) linking the effects of mosquito control to disease outcomes, and (4) having limited information about mosquito control entities.

Federal agencies faced challenges related to the cyclic nature of mosquito-borne diseases, including recruiting and maintaining expertise. According to CDC, when the disease fades, the jobs and resources also go away, so that the next time the disease appears, staff must be retrained or new staff trained. CDC officials also told us that mosquito control needs vary with seasonal cycles, resulting in periods of several months that require more resources followed by some periods when little or no resources are needed.

CDC also faced challenges in communicating the presence of mosquitoes in a manner that was clear and useful to different groups, such as mosquito control entities and the general public. CDC distributed maps of the estimated potential range of the primary Zika virus mosquito vectors on its webpages and in guidance, but imprecision in the maps can lead to confusion, according to some mosquito control officials. According to CDC officials, the maps allowed states to determine the level of effort needed for more precise mosquito surveillance as well as to show the public where they may encounter certain mosquito species. One mosquito control official told us of confusion about CDC's maps resulting from people failing to look at the qualifications stated in the map captions and mistakenly concluding that an entire state was infested with Zika virus vector mosquitoes. Further, detailed information about how the maps were created, including data sources and assumptions, was not posted on the CDC website or in documentation associated with the map. According to *Standards for Internal Control in the Federal Government*, management should use quality information to achieve the agency's objectives and should select appropriate methods to communicate externally the necessary quality information to achieve those objectives.[10] This includes selecting appropriate methods to communicate externally, considering factors such as the intended recipients and the nature of the information being communicated.

[10]GAO-14-704G.

Regarding information presented on CDC maps, experts we interviewed suggested including more details, such as collection records, measures of the stability of the mosquito populations, and areas of risk for transmission of mosquito-borne diseases. Without such context, CDC's maps could generate confusion about mosquito presence, resulting in concern among residents and public relations challenges, among other things. In our report we recommended that CDC provide details such as collection records, dates, and data limitations on posted and disseminated mosquito distribution maps to better inform mosquito control experts and the general public. HHS agreed with this recommendation.

CDC faced challenges in determining whether mosquito control efforts are associated with the reduction of mosquito-borne disease. For example, mosquito control entity officials told us that the entities' mosquito control efforts are not directly linked to disease reduction. Other challenges to analyzing the relationships between mosquito control methods and disease reduction include the dependence of transmission on factors such as weather, human susceptibility, and immunity.

CDC's capacity to develop a national strategy for mosquito control depends on its knowledge of mosquito control entities and their capabilities. We found that CDC relied on external sources to compile a list of mosquito control entities. CDC staff told us this list is likely to capture the larger, well-funded entities but may miss some smaller ones. Further, mosquito control capabilities in the United States vary by geographic area. A mosquito control official we interviewed agreed that variability in mosquito control entity capacities is significant. This variability makes it more challenging for CDC to determine the status of mosquito control efforts in different regions of the United States and to identify regions that may need technical guidance or assistance.

In conclusion, federal agencies can provide important information that can help users compare diagnostic tests and assist mosquito control efforts implemented at the state and local levels. Information on performance characteristics presented in each diagnostic test product label was not consolidated across available tests, were not consistently reported for diagnostic tests, and the identity of the comparator test was not listed on some labels, making it difficult for users to make informed decisions about which test to use or recommend to patients. The information that CDC included in its maps did not include sufficient details about its estimates of potential distribution of mosquitoes that can carry the Zika virus, which

made it difficult for mosquito control experts and the public to correctly interpret and use such data.

CDC developed the first two authorized diagnostic tests for the Zika virus and offers these tests to public health laboratories but not to some manufacturers. Such manufacturers additionally encountered difficulty acquiring authorized tests from other manufacturers. Without a clear and transparent process for distributing CDC-developed diagnostic tests to manufacturers, the agency may not be able to develop the capacity of the commercial sector to be able to meet the needs during an outbreak.

Chairman Murphy, Ranking Member DeGette, and Members of the Subcommittee, this concludes my prepared statement. I would be happy to respond to any questions you may have.

For questions about this statement, please contact Timothy M. Persons, Ph.D., Chief Scientist, at (202) 512-6412 or personst@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this statement. Individuals making key contributions to this statement include Sushil Sharma, Ph.D, Dr.PH, (Assistant Director), Ashley Grant, Ph.D, MPH, Hayden Huang, Ph.D., Amber Sinclair, Ph.D., and Penny Pickett, Ph.D.

GAO's Mission	The Government Accountability Office, the audit, evaluation, and investigative arm of Congress, exists to support Congress in meeting its constitutional responsibilities and to help improve the performance and accountability of the federal government for the American people. GAO examines the use of public funds; evaluates federal programs and policies; and provides analyses, recommendations, and other assistance to help Congress make informed oversight, policy, and funding decisions. GAO's commitment to good government is reflected in its core values of accountability, integrity, and reliability.
Obtaining Copies of GAO Reports and Testimony	The fastest and easiest way to obtain copies of GAO documents at no cost is through GAO's website (http://www.gao.gov). Each weekday afternoon, GAO posts on its website newly released reports, testimony, and correspondence. To have GAO e-mail you a list of newly posted products, go to http://www.gao.gov and select "E-mail Updates."
Order by Phone	The price of each GAO publication reflects GAO's actual cost of production and distribution and depends on the number of pages in the publication and whether the publication is printed in color or black and white. Pricing and ordering information is posted on GAO's website, http://www.gao.gov/ordering.htm. Place orders by calling (202) 512-6000, toll free (866) 801-7077, or TDD (202) 512-2537. Orders may be paid for using American Express, Discover Card, MasterCard, Visa, check, or money order. Call for additional information.
Connect with GAO	Connect with GAO on Facebook, Flickr, LinkedIn, Twitter, and YouTube. Subscribe to our RSS Feeds or E-mail Updates. Listen to our Podcasts. Visit GAO on the web at www.gao.gov and read The Watchblog.
To Report Fraud, Waste, and Abuse in Federal Programs	Contact: Website: http://www.gao.gov/fraudnet/fraudnet.htm E-mail: fraudnet@gao.gov Automated answering system: (800) 424-5454 or (202) 512-7470
Congressional Relations	Katherine Siggerud, Managing Director, siggerudk@gao.gov, (202) 512-4400, U.S. Government Accountability Office, 441 G Street NW, Room 7125, Washington, DC 20548
Public Affairs	Chuck Young, Managing Director, youngc1@gao.gov, (202) 512-4800 U.S. Government Accountability Office, 441 G Street NW, Room 7149 Washington, DC 20548
Strategic Planning and External Liaison	James-Christian Blockwood, Managing Director, spel@gao.gov, (202) 512-4707 U.S. Government Accountability Office, 441 G Street NW, Room 7814, Washington, DC 20548

Mr. MURPHY. Thank you.

Dr. Petersen, you're recognized for 5 minutes.

STATEMENT OF LYLE R. PETERSEN

Dr. PETERSEN. Thank you, Chairman Murphy, Ranking Member DeGette, and members of the subcommittee, for the opportunity to discuss CDC's response to the Zika virus outbreak. I'm Dr. Lyle Petersen, Director of the Division of Vector-Borne Diseases in CDC's National Center for Emerging and Zoonotic Infectious Diseases. I also had the opportunity to serve as CDC's Zika response incident manager throughout most of 2016, and I would like to make three key points to start.

First, it has been almost 17 months since CDC activated its emergency operation center for Zika, and it is clear that this outbreak has resulted in CDC's most complex emergency response to date.

Second, we have accomplished a great deal very rapidly, in large part due to support in supplemental funding from Congress. However, we still have much to learn, and much remains to be done.

Third, Zika remains a significant threat today, particularly to pregnant women and their infants. We need to remain ready for Zika and for mosquito-borne diseases in general as we expect more to emerge in the upcoming years.

Looking at the response to date, we have learned a tremendous amount about a little known virus in a very short amount of time. First, we confirmed the link between Zika virus infection during pregnancy and severe birth defects, including microcephaly. Along with State and local territorial partners, we have begun to quantify the risk of birth defects, which we now know affects about 10 percent of fetuses exposed to Zika. We also discovered that Zika can be sexually transmitted, and we also have better information about the geographic range of mosquitoes that can spread Zika.

The support efforts on the ground: CDC has provided $251 million in Zika-specific funding to State, local, and territorial health departments, as well as ongoing CDC technical assistance.

I want to briefly turn to one of the most challenging aspects of the response: diagnostic testing for Zika. Because Zika's impact on pregnancies can be devastating, CDC has recommended testing for all pregnant women who live in or have traveled to an area at risk for Zika. When the emergency response began in January 2016, women did not have access to even one Zika test authorized for clinical use. However, by March 2016, Emergency Use Authorizations were in place for two CDC-developed tests, allowing for distribution of these testing resources to State laboratories while also sharing information with manufacturers that were developing their own tests. CDC remains committed to improving Zika diagnostics, so that they're faster and more accurate, and will continue to share information with public health and commercial laboratories as it becomes available.

So, as we approach summer, it is impossible to predict with certainty what we will see in the way of local transmission of Zika. However, we anticipate that the Zika virus will continue to circulate indefinitely in most regions in the Americas where it has been introduced. We will undoubtedly continue to see pregnant

women test positive for Zika virus in both States and U.S. territories.

We expect fewer Zika cases this year in some areas outside of the 50 States, such as Puerto Rico, simply because a significant proportion of the population was infected in 2016 and is no longer susceptible to infection.

Within the continental United States, local outbreaks remain possible, such as those seen in this past year in Florida and Texas. Any local outbreaks will, of course, be of deep concern, and we must be prepared for different scenarios, including more extensive transmission.

Finally, we have learned to expect the unexpected when it comes to Zika. So it is critical to remain vigilant and sustain our response efforts.

So, in closing, CDC, our sister agencies within HHS, and our partners have accomplished much, but we continue to face numerous challenges. One major challenge is to continue learning as much as we can about Zika. We know of the most devastating effect of microcephaly, but we need to follow the development of these babies to understand the full spectrum of long-term effects.

Also, we can expect Zika to circulate for many years. So we must be prepared to scale up Zika prevention efforts at any time. Even after a Zika vaccine becomes available, other Zika prevention efforts, including surveillance and mosquito control, will be required.

Lastly, the emergence of mosquito-borne diseases is accelerating. So we must address the threat of vector-borne diseases systematically and continually, rather than episodically and sporadically.

Thank you again for the opportunity to appear before you today.

[The prepared statement of Dr. Petersen follows:]

May 23, 2017

Witness: Dr. Lyle Petersen, Director, Division of Vector-Borne Diseases and former Zika Response Incident Manager

Testimony: House Energy and Commerce Committee, Subcommittee on Oversight and Investigations

Introduction

Good morning Chairman Murphy, Ranking Member DeGette, and members of the Subcommittee. Thank you for the opportunity to testify before you today on the Centers for Disease Control and Prevention's (CDC's) ongoing efforts to prepare for and respond to the Zika virus outbreak, which continues to threaten the United States and the rest of the Americas. CDC is the nation's health protection agency, working 24-7 to save lives and protect people.

It has been about 17 months since CDC first activated its Emergency Operations Center to protect the nation and U.S. territories against the threat of Zika. As the director for the Division for Vector-Borne Diseases for CDC's National Center for Emerging and Zoonotic Infectious Diseases, I had the opportunity to serve as the incident manager for the Zika response for most of 2016. This response has been the most complex emergency response to date. It has required expertise from across the agency, including experts in pregnancy and birth defects, mosquito control, laboratory science, travelers' health, virology, transfusion medicine, sexually transmitted diseases, and communication science. We have learned a great deal very rapidly about a surprising infectious disease. For the very first time, we have found that a virus transmitted through the bite from a mosquito can cause birth defects. However, we still have much to learn and Zika remains a significant threat, particularly to pregnant women and their infants.

Thanks in significant part to the Zika supplemental funding provided by Congress, CDC has taken important steps forward. First, we established a causal link between Zika virus infection during

pregnancy and microcephaly, including serious brain abnormalities. In early 2016, CDC established Zika pregnancy registries in collaboration with state, tribal, territorial, and local health departments to rapidly gather information about risks posed by Zika virus infection, including whether there are certain times during pregnancy when the risk of birth defects from exposure to Zika is greatest. These registries capture information about pregnant women with Zika and their babies. While the Zika pregnancy registries contain information on women who have been tested for Zika and are known to be infected, we know that not all pregnant women exposed to Zika will be tested during the relatively narrow time period when we can identify Zika infections. Therefore, CDC also established rapid birth defects surveillance to identify the same Zika-associated birth defects in babies whose mothers might not have been tested for Zika in the time period when maternal infection could be identified. The combination of the pregnancy registries and rapid birth defects surveillance are providing critical data for public health officials and clinicians, and these combined systems are the only way to identify all the babies affected by congenital Zika virus infection.

We also determined that Zika infection can cause a form of paralysis known as Guillain-Barré Syndrome, which can also lead to respiratory failure and death if not treated aggressively. We found that in addition to being transmitted through the bite of a mosquito, Zika can also be sexually transmitted. CDC has been rapidly developing both molecular and serologic tests for Zika and received Emergency Use Authorizations (EUA) from the Food and Drug Administration (FDA) for their clinical use. At the beginning of 2016, no state had the capacity to test for Zika. Today, 49 states, D.C., and Puerto Rico have this testing capacity. Together with CDC's Laboratory Response Network, CDC has conducted over 160,000 Zika tests. CDC has also issued over 60 travel notices to inform the public, especially pregnant women, about international destinations and U.S. territories and states where Zika virus is circulating.

Partnerships with and support for state and local health departments has been essential to help address the threat of Zika. To date, CDC has provided $251 million in Zika-specific funding directly to state, local, and territorial health departments through grants. In addition to direct funding, CDC has awarded funding that directly supports state, local, and territorial efforts, including support to partner organizations, vector-borne disease regional centers of excellence, and the Puerto Rico Vector Control Unit. All of CDC's supplemental funds will be obligated by September 30, 2017. These financial resources are coupled with technical support to states and territories through rapid response teams, as well as laboratory, epidemiologic, entomologic, field investigation, and data management support. In addition, CDC is providing on-going, in-depth support to Florida, Texas, and U.S. territories, where public health officials have found themselves battling local transmission of mosquito-borne Zika.

Collaboration with our sister agencies has also been critical throughout this response. CDC has been working closely with multiple agencies within the Department of Health and Human Services, including the Office of the Assistant Secretary for Preparedness and Response (ASPR) and its Biomedical Advanced Research and Development Authority (BARDA), the National Institutes of Health (NIH), and the FDA who are all here today. CDC is also working with partners across the U.S. Government, including the Department of State, the United States Agency for International Development (USAID), the Department of Homeland Security (DHS), the Department of Veterans Affairs (VA), and the Environmental Protection Agency (EPA) to communicate with travelers and health care providers, update travel alerts and clinical guidance, further our understanding of the Zika virus, and develop improved mosquito-control methods. Finally, CDC has collaborated with a range of private sector and non-profit partners, including organizations ranging from the March of Dimes to public health associations, like the Association of State and Territorial Health Officials.

What We Expect in 2017

It is impossible to predict with certainty what we will see in the way of local transmission of Zika, but here is what CDC's scientists anticipate:

- Zika virus will continue to circulate in most regions in the Americas where it has been introduced.
- Over the past year, an average of 30 to 40 pregnancies per week with laboratory evidence of possible Zika virus infection have been reported from the 50 states, and a much higher number from the U.S. territories. Dozens of new cases in pregnant women continue to be reported each week.
- We expect fewer Zika cases in 2017 in some areas outside of the continental U.S., such as Puerto Rico, because a significant proportion of the population was infected in 2016 and is no longer susceptible to infection.
- Within the continental U.S., local outbreaks remain possible, such as those seen this past year in Florida and Texas. Zika outbreaks in the U.S. mainland may be localized due to protective factors like air conditioning, window screens, and less dense living conditions; however, we must be prepared for local outbreaks and different scenarios -- including more extensive transmission.
- There are about 40 million people traveling between the continental U.S. and Zika-affected areas each year. Therefore, all U.S. jurisdictions must continue to be prepared to evaluate, test, and manage patients with potential Zika virus infection, particularly pregnant women.

With these expectations in mind, CDC continues to recommend that those living in areas of local Zika transmission and those traveling to areas of local Zika transmission take steps to prevent mosquito bites and prevent sexual transmission. At the request of state and local public health officials, CDC will

continue to send emergency response teams to states and territories with Zika outbreaks. CDC will also continue to provide reference and surge laboratory capacity for the nation; continue registries to track Zika-affected pregnancies and births; help states deploy and target effective mosquito control; and support timely, accurate, and effective communications to the public and health care providers. In order to cultivate capacity and innovation in the area of vector control, CDC will work with our newly awarded vector-borne disease regional centers of excellence to generate the research, knowledge, and capacity needed to prepare the nation for ongoing vector threats, such as Zika. We will also collectively work with our commercial partners on diagnostic and vector control innovation. Finally, to help facilitate access to the specialty care that is needed by infants affected by Zika, CDC has established a provider referral network called Zika Care Connect that includes a hotline to help families find specialists and a website launched last month. Even when a vaccine becomes available and deployed, these CDC investments will remain critical to protect U.S. states and territories against Zika and other mosquito-borne threats.

Zika Virus Diagnostic Testing

The Zika virus has presented multiple diagnostic challenges, and while we have overcome some of these, several key challenges remain.

One of our first challenges was that while Zika infection typically causes a mild illness or no symptoms at all, the impact of Zika on pregnancies can nonetheless be significant. Therefore, CDC currently recommends testing for all pregnant women who live in or travel to an area with risk of Zika that has a CDC Zika travel notice. At the beginning of the emergency response in January 2016, women did not have access to even one Zika test that was approved for clinical use. However, within three months of initiating the emergency response CDC received EUAs for both a molecular test (Zika nucleic acid test) to detect Zika in the first two weeks after infection and a serological test (IgM) to detect

infection for weeks to months after an infection. Once FDA authorized emergency use of these tests, CDC worked to distribute them rapidly to state laboratories and ensured state laboratories were proficient in their use, while also sharing information about test performance with manufacturers that were developing their own tests. This allowed others to benchmark their tests against the first FDA-authorized Zika tests. Today there are 12 Zika nucleic acid tests with emergency use authorizations and 49 state public health laboratories have Zika nucleic acid testing capacity. Forty-six states have the capacity to conduct CDC's IgM test, known as MAC-ELISA, and two more IgM tests have since received EUAs. To further increase testing capacity at the height of demand in 2016, CDC arranged for referral labs to provide MAC-ELISA testing. These labs continue to provide Zika testing support, and now have the option of either using the MAC-ELISA or using commercially available tests now available under EUA.

CDC remains committed to making ongoing improvements to Zika diagnostics and will continue to share information with public health and commercial laboratories about test performance for tests that are approved for clinical use. Fortunately, FDA's EUA process allows for updates to be made to diagnostic tests as the scientific community makes discoveries that can be used to improve test performance. This ensures that clinicians have the best possible information to counsel their patients. As CDC has made these improvements, the Agency has worked to quickly update laboratory guidelines and notify public health partners and manufacturers of these changes. This includes updating the information on CDC diagnostic test inserts, the information posted on our website for CDC-developed tests that are FDA-authorized for distribution, and published and posted testing guidance.

CDC also works with states to ensure that they have sufficient proficiency to perform CDC's tests. Additionally, CDC provided laboratory surge support to states and territories during periods of high testing volume, so that patients received information about their health status as quickly as

possible. This process has been a major challenge, but CDC remains committed to ongoing communication with and support of our public health partners in preventing the spread of Zika.

Despite the progress CDC has made on the diagnostic landscape, there is still work to do. CDC will continue to work towards diagnostic test improvements that can detect current or recent Zika infection faster and with greater accuracy. This can help decrease the testing burden on the public health system and ensure that patients and their doctors have timely, accurate information. Additionally, sensitive serological tests are needed that can detect recent or previous Zika virus infection without cross-reacting with other flaviviruses, like dengue virus. This cross reactivity makes it difficult to counsel pregnant women about previous exposure to Zika virus. Finally, we need to better understand how long Zika virus can remain in body fluids such as blood and semen, which can inform our laboratory guidance as well as our prevention messaging.

Tracking the Zika Virus

As CDC continues to advance our ability to detect Zika in patients, we also continue to improve our ability to monitor the spread of Zika in communities. Zika virus is a nationally notifiable disease, meaning states and territories report cases of the virus to CDC. CDC conducts multi-faceted surveillance for Zika and other arboviruses through ArboNET, an integrated network that funds 49 states, the Commonwealth of Puerto Rico, and six large municipalities to conduct human case investigations, collect and test mosquitoes, and perform laboratory analysis on arboviruses including Zika, through our Epidemiology and Laboratory Capacity cooperative agreement. Our most recent surveillance data show that we have documented 36,583 cases of Zika virus disease in the U.S. territories and 5,282 in U.S. states and DC. Of these cases, we have identified 224 cases of Zika in Florida and Texas due to local mosquito transmission. CDC has also documented 3,795pregnant women with laboratory evidence of Zika virus infection in U.S. territories and 1,845 in U.S. states and D.C.

Of the nearly 1,000 births in 2016 recorded in the Zika pregnancy registries, 51 had a Zika-associated birth defect, mostly serious brain abnormalities and microcephaly. CDC has found that among pregnant women with confirmed Zika virus infection, about 10 percent of their fetuses and babies were affected by serious Zika-associated birth defects, primarily serious damage to their brains. For those with Zika infections in the first trimester, 15 percent of fetuses and babies had Zika-associated birth defects. The Zika pregnancy registries have also allowed CDC to identify some gaps in care. Based on data reported to the registries, only about one in four babies born to women with Zika virus infection during pregnancy are receiving the recommended brain imaging after birth. Some brain abnormalities are only identified with brain imaging, suggesting that the impact of Zika on babies born to mothers infected with the virus may be underestimated.

In addition to monitoring the impact of Zika, CDC scientists are also monitoring the vector itself in order to better target prevention resources and best support state and local vector control efforts. Documenting the national and local range of mosquito species is an important public health activity because it can inform vector control activities, allowing for the selection of species-appropriate interventions. Zika virus is transmitted primarily by the *Aedes aegypti* mosquito, but also in some circumstances by other species such as the *Aedes albopictus* mosquito. Both of these mosquito species are spreading to new areas within the United States. Using county collection records, CDC has created maps that reflect which counties have documented these species and overlaid the best estimated range of these mosquitoes. However, because we must rely on voluntary county collection records of where mosquito species have been identified, we have been careful to caution the public that these maps reflect our best estimate of where mosquitoes could potentially live. As CDC continues to publish additional information about the range of *Aedes* species mosquitoes, we will continue to communicate the limitations of these reports. Importantly, CDC's investment in the mosquito surveillance system MosquitoNet will allow for more extensive collection of this information, which is intended to improve

the precision of our estimates and provide new information about insecticide resistance in communities across the country.

Conclusion

In closing, the emergence and reemergence of diseases spread by mosquitoes and other insects is exemplified but not limited to the present Zika outbreak. With the spread of the *Aedes aegypti* and other vector mosquito species, mosquito-borne outbreaks will continue and cannot be expected to occur in isolation of one another. The Commonwealth of Puerto Rico and Hawaii were already responding to outbreaks of dengue when Zika virus arose as an urgent public health threat. Alarmingly, the emergence of mosquito-borne diseases appears to be accelerating. Over the past few decades, we have seen a resurgence of dengue and the introduction and spread of West Nile virus, chikungunya virus, and now Zika virus into the Western Hemisphere. Out of the more than 200 known arboviruses in existence, CDC knows of 86 that can cause illness in people. It is very hard to determine which one might next cause an epidemic. However, we know that mosquito-borne diseases will continue to be introduced. Because of this, we need to address the threat of vector-borne diseases systematically, rather than episodically.

Thank you again for the opportunity to appear before you today and for your support of our fight to protect the U.S. and its territories from the threat of Zika virus. I appreciate your attention to this continuing outbreak and I look forward to answering your questions.

Mr. MURPHY. Thank you, Dr. Petersen.
Dr. Borio, you're recognized for 5 minutes.

STATEMENT OF LUCIANA BORIO

Dr. BORIO. Good morning, Chairman Murphy, Ranking Member DeGette, and members of the subcommittee. I greatly appreciate the opportunity to be here today and tell you about FDA's ongoing actions to respond to the Zika virus outbreak.

FDA plays a central role in the Nation's response to public health emergencies. In addition to responding to Zika, our teams are fully engaged in responding to the H7N9 influenza virus that has emerged in China and the most recent outbreak of Ebola in the DRC.

Since the 2009 influenza pandemic, multidisciplinary teams have worked collaboratively across the agency to respond to a number of public health crises. They bring vision, experience, and expertise to their work at hand, which, backed by FDA's flexible regulatory framework, allows for us to make important contributions to global health security. So today I'm here to assure you that FDA remains fully engaged with our partners to help minimize the impact of Zika virus.

We are focused on four work streams: supporting the expedited development and availability of diagnostic tests, investigational vaccines, and therapies; working to advance innovative strategies for vector control; keeping the Nation's blood supply safe; and protecting the public from fraudulent products. And let me tell you more about some of these efforts.

At the start of this outbreak, there were no clinical diagnostic tests for Zika available for use. We have worked urgently with our colleagues at the CDC to make Zika tests rapidly available. In February and March of 2016, FDA authorized the use of two CDC-developed tests under our Emergency Use Authorities. We also immediately began working interactively with interested commercial manufacturers. We granted an EUA for the first commercial test in April of 2016.

FDA has taken several proactive steps to help advance the development and availability of Zika tests. We developed and made available to developers fillable forms that lay out the data requirements for an EUA. Our scientists generated reference materials to help developers assess the analytical performance of their molecular diagnostic tests. And our scientists in collaboration with both establishments are developing reference materials to help developers of serological tests.

There's some very complex scientific challenges associated with developing Zika diagnostic tests, as you heard from Dr. Petersen. This is especially true for serological tests designed to detect the presence of antibodies to Zika due to issues of cross-reactivity with other flaviviruses like dengue and yellow fever. FDA continues to work interactively with dozens of developers as they try to overcome these challenges.

FDA has held more than 15 face-to-face meetings, 150 teleconferences, and more than 3,500 written exchanges with developers to help guide their programs. This highly interactive approach has been extremely successful. To date, we have authorized the use of

16 diagnostic tests for Zika. And even after an EUA is issued, FDA and developers continue to work interactively to optimize the authorized tests. We have issued 21 amendments to EUAs designed to improve product performance, and thanks to these efforts, a broad range of Zika tests with a broad range of performance are now available in laboratories throughout the U.S.

As you heard from my colleague, Dr. Petersen, CDC projects that Zika will become established in the Americas, posing a continuing threat, especially to pregnant women. One of our highest priorities is to facilitate the development and availability of an effective vaccine. We are working closely with the NIH, BARDA, and the private sector on this, and there's reason for optimism, with several vaccine's candidates progressing at a rapidly expedited pace.

In addition, FDA continues to work with blood collection establishments to protect the safety of the blood supply. In August of 2016, after careful consideration of the evolving scientific and epidemiological data, we issued guidance recommending that all States and U.S. territories screen blood with an investigational screening test.

We are very appreciative of blood collection establishments' efforts to implement universal screening for Zika across the U.S. in a timely fashion. To date, the screening has been prevented nearly 400 infected donations from entering the blood supply.

The FDA remains fully committed to sustaining our deep engagement and aggressive activities to support a robust response to Zika.

In closing, I would like to recognize and thank the more than 500 staff members at the FDA who approached this work with incredible dedication, innovation, and expediency. Thank you, and I'm happy to answer your questions later.

[The prepared statement of Dr. Borio follows:]

TESTIMONY

OF

LUCIANA BORIO, M.D.

CHIEF SCIENTIST (ACTING)

FOOD AND DRUG ADMINISTRATION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

HOUSE ENERGY AND COMMERCE COMMITTEE

U.S. HOUSE OF REPRESENTATIVES

U.S. PUBLIC HEALTH RESPONSE TO THE ZIKA VIRUS: CONTINUING CHALLENGES

MAY 23, 2017

RELEASE ONLY UPON DELIVERY

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

INTRODUCTION

Good morning Chairman Murphy, Ranking Member DeGette, and members of the Subcommittee. I am Dr. Luciana Borio, Acting Chief Scientist at the Food and Drug Administration (FDA). Thank you for the opportunity to appear today to discuss FDA's actions in response to the Zika virus outbreak.

Zika virus was first identified in 1947 in Uganda. Since then, sporadic cases and a few outbreaks have been recognized in a number of locations, including parts of Africa, Asia, and the Pacific. However, the situation has changed dramatically since May 2015, when the first local transmission of Zika virus in the Americas was confirmed in Brazil. According to the World Health Organization, from 2015 through March 10, 2017, 61 countries and territories—including the United States, the Commonwealth of Puerto Rico, the U.S. Virgin Islands, and American Samoa—have had ongoing transmission following a new introduction of Zika virus or with a reintroduction into an area where transmission had been interrupted.[1] Additionally, 13 countries have reported evidence of person-to-person transmission, 31 countries or territories have reported microcephaly and other central nervous system malformations that are potentially associated with Zika virus infection, and 23 countries or territories have reported an increase in the incidence of Guillain-Barre Syndrome (GBS) or laboratory confirmation of Zika virus infection among GBS cases.[1]

[1] WHO Zika Virus Situation Report, 10 March 2017; http://apps.who.int/iris/bitstream/10665/254714/1/zikasitrep10Mar17-eng.pdf?ua=1

In the United States, there have been 5,282 Zika virus disease cases reported in the states [5,010 cases in travelers returning from affected areas, 224 cases acquired through presumed local mosquito-borne transmission in Florida (218 cases) and Texas (6 cases), and 48 cases acquired through other routes, including sexual transmission] and 36,583 Zika virus disease cases reported in the US territories [143 cases in travelers returning from affected areas and 36,440 cases acquired through presumed local mosquito-borne transmission] as of May 17, 2017.[2] As of May 09, 2017, there are 1,845 pregnant women in the states and District of Columbia and 3,795 pregnant women in the US territories with laboratory-reported evidence of possible Zika virus infection.[3]

FDA RESPONSE TO THE ZIKA VIRUS OUTBREAK

FDA has taken several steps to rapidly respond to the Zika virus outbreak and remains actively engaged with other components of the Department of Health and Human Services (HHS)—including the Office of the Assistant Secretary for Preparedness and Response (ASPR) and its Biomedical Advanced Research and Development Authority (BARDA), the National Institutes of Health (NIH), and the Centers for Disease Control and Prevention (CDC)—as well as with partners across the U.S. Government, the private sector, and the international community to minimize the impact of this outbreak. FDA's primary areas of activity include: (1) supporting the development and availability of diagnostic tests that may be useful for identifying the presence of, or prior exposure to, Zika virus; (2) providing advice and consultation to facilitate rapid development of investigational vaccines and therapeutics; (3) advancing the use of innovative

[2] CDC 2017 Case Counts in the US; https://www.cdc.gov/zika/geo/united-states.html, 2016 Case Counts in the US; https://www.cdc.gov/zika/reporting/2016-case-counts.html, and 2015 Case Counts in the US; https://www.cdc.gov/zika/reporting/2015-case-counts.html.
[3] CDC Pregnant Women with Any Laboratory Evidence of Possible Zika Virus Infection in the United States and Territories; https://www.cdc.gov/zika/geo/pregwomen-uscases.html

strategies under FDA's regulatory authorities to help suppress the population of Zika virus-carrying mosquitoes; (4) protecting the public from fraudulent products that claim to prevent, diagnose, treat, or cure Zika virus disease; and (5) protecting the safety of the nation's blood supply and human cells, tissues, and cellular and tissue-based products (such as corneas, bone, skin, heart valves, and semen) used for medical, surgical, or reproductive procedures.

Diagnostic Tests

At the start of the Zika virus outbreak in the Americas, there were no diagnostic tests for the detection of Zika virus authorized for use in the United States. FDA worked with CDC, which was developing diagnostic tests, to make Zika diagnostic tests rapidly available. FDA was able to authorize the use of two CDC tests under FDA's Emergency Use Authorization (EUA) authority in February and March of 2016. FDA also—in keeping with FDA's normal practice for responding to emerging infectious disease outbreaks—reached out to diagnostic manufacturers to encourage them to develop needed diagnostic tests for Zika virus. FDA immediately began working interactively with manufacturers interested in developing diagnostic tests for Zika virus to help accelerate development programs—including clarifying EUA data requirements for the Zika diagnostic tests—and to ensure that their tests are properly validated before they are used to inform patient care. FDA granted an EUA for the first commercial test in April 2016.

FDA has taken several proactive steps to help advance the development of diagnostic tests for Zika virus. For example, FDA developed and made available EUA review templates delineating data requirements for a Zika virus diagnostic EUA. FDA has fulfilled more than 100 requests for the EUA templates. In addition, to help Zika diagnostic manufacturers develop nucleic acid testing-based diagnostic devices, FDA created Zika virus reference materials that are available to

Zika diagnostic manufacturers that have a pre-EUA submission with FDA and have established the analytical performance of their assay.[4] FDA has fulfilled 17 requests for the reference materials.

FDA has continued to work interactively with Zika virus diagnostic manufacturers throughout the product development process to address scientific challenges, review data, and provide feedback based on the latest available scientific information. For example, FDA has had more than 15 face-to-face meetings, 150 teleconferences, and more than 3,500 emails with diagnostic developers or Zika experts to support the development of Zika diagnostics. This collaboration has been extremely successful, and to date, FDA has authorized the use of sixteen diagnostic tests for Zika virus under FDA's EUA authority—13 nucleic acid testing-based tests to diagnose active infection (12 of which are currently available[5]) and 3 serological tests to assess whether individuals who may have recently been exposed to Zika had actually been infected. It is important to note that, as a result of these efforts, diagnostic tests for Zika virus are now available in laboratories throughout the United States including automated, high throughput tests. The serological tests to assess whether individuals who may have been exposed to Zika recently had actually been infected are especially important for women given the link between Zika virus infection and congenital Zika syndrome, including microcephaly and other birth defects, in babies of mothers who were infected with Zika virus during their pregnancy.

FDA continues to work with diagnostic manufacturers once their tests are authorized under EUA to further product development, improve product performance, and make sure that authorized

[4] FDA has created an email account specifically for requesting the EUA review templates (CDRH-ZIKA-Templates@fda.hhs.gov).
[5] At the request of Roche Molecular Systems, Inc., on March 13, 2017, FDA revoked the EUA for emergency use of the company's *LightMix® Zika rRT-PCR Test* that was issued on 26 August 2016, reducing the number of tests to diagnose active infection to 12.

tests continue to meet EUA standards and public health needs. For example, FDA has issued 21 amendments to EUAs for the authorized Zika diagnostic tests—upon request from the product manufacturers—to add additional instruments or specimen types for testing. In addition, FDA is continuing to work to help advance the development of diagnostic tests for Zika virus. For example, FDA is supporting the validation and use of a World Health Organization reference panel to be developed into an international standard for serological assays. FDA also monitors the performance of Zika diagnostic tests authorized under EUA and works with manufacturers and laboratory personnel to quickly resolve any issues that may arise. Toward that end, FDA has established an email account that laboratory personnel using Zika diagnostic assays under EUA are encouraged to use to report performance concerns directly to FDA (CDRH-EUA-Reporting@fda.hhs.gov), in addition to reporting concerns to the manufacturer.

All information about diagnostic tests for Zika virus authorized under EUA, such as letters of authorization, labeling that includes the tests' performance data, and fact sheets for patients and health care providers, are readily available on the FDA website.[6]

Vaccines and Therapies

There are no vaccines or treatments for Zika virus at this time. Development programs are in the relatively early stages, but several vaccine candidates continue to progress at an expedited pace. FDA is actively engaged with NIH and BARDA, the international community, and product developers to help accelerate development programs. FDA is working with medical product developers to provide technical support and clarify regulatory and data requirements necessary to move products forward in development as quickly as possible. One of our highest priorities is to facilitate the development and availability of an effective Zika virus vaccine as quickly as

[6] Zika Virus Emergency Use Authorizations; https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika

possible and we are working closely with NIH, BARDA, CDC, and the private sector on this. Although therapeutic development proposals are generally at an earlier stage than for vaccines, FDA has also engaged in preliminary discussions of potential approaches to the development of therapeutics and is open to ongoing interactions to provide input on such development proposals.

Vector Control

In the United States, mosquito control is typically achieved by a multi-faceted approach that relies on a range of tools, including surveillance of mosquito activity, reduction in breeding sites, and the use of chemical and biological control methods. FDA's involvement in mosquito control is through the oversight of products that help suppress the population of virus-carrying mosquitoes that fall under FDA's regulatory authorities. With respect to Zika virus, there has been public discussion of a new method to potentially help control mosquito populations through the use of a genetically engineered (GE) line of the mosquito *Aedes aegypti* (OX513A) developed by Oxitec, Ltd. The release of male Oxitec GE mosquitoes is intended to cause suppression of the mosquito population in a release area over time because the offspring resulting from the mating of male GE mosquitoes with wild-type females do not develop to adulthood.

FDA reviewed information in an Investigational New Animal Drug (INAD) file from Oxitec Ltd. regarding the potential use of the company's GE mosquito with the intent of suppressing the population of *Aedes aegypti* mosquitoes at the release site in Key Haven, Florida.[7] On August 5, 2016, FDA completed the environmental review for a proposed field trial of Oxitec's GE

[7] FDA ordinarily cannot acknowledge or discuss INAD files due to confidentiality concerns; however FDA is able to do so in this case because Oxitec has publicly announced that they have opened an INAD file.

mosquitoes in Key Haven, Florida, and published a final environmental assessment—or EA—and finding of no significant impact—or FONSI—stating that the proposed field trial will not have significant impacts on the environment. This enabled the field trial to proceed, provided all other local, state, and federal requirements are met. Ultimately, Oxitec, together with its local partner, the Florida Keys Mosquito Control District, decided not move forward with the Key Haven field trial as the result of a November 8, 2016, referendum on the use of GE mosquitoes that found Key Haven residents did not support the trial. Since then, FDA and Oxitec have maintained an open line of communication and FDA stands ready to promptly review any submissions should, for example, Oxitec decide to pursue a field trial in another location.

Meanwhile, in January 2017, FDA issued draft guidance (developed in coordination with the Environmental Protection Agency (EPA)) that clarifies that mosquito-related products intended to function as pesticides by preventing, destroying, repelling, or mitigating mosquitoes for population control purposes are not "drugs" under the Federal Food, Drug, and Cosmetic Act (FD&C Act). If the guidance is finalized, these products will be regulated by EPA as "pesticides" under the Federal Insecticide, Fungicide, and Rodenticide Act. FDA would continue to have jurisdiction over mosquito-related products that otherwise meet the FD&C Act drug definition, such as those intended to prevent, treat, or cure a disease or to reduce the viral or pathogen load in a mosquito. The 30-day public comment period for the draft guidance closed on February 21, 2017. FDA is currently considering the comments.

Fraudulent Product Claims

Unfortunately, during emerging infectious disease outbreaks such as this, fraudulent products that claim to prevent, treat, or cure a disease frequently appear on the market. FDA is actively

monitoring for fraudulent products and false product claims related to Zika virus and will implement enforcement actions, as warranted, to protect the public health.

Blood Supply and Tissue Safety

One of FDA's first actions in response to the Zika virus outbreak was to take important steps to help protect the safety of the blood supply. FDA issued guidance in February 2016 that recommended the deferral of individuals from donating blood if they had been to areas with active Zika virus transmission, were potentially exposed to the virus, or had a confirmed infection. The guidance also recommended that areas with active Zika virus transmission, like Puerto Rico, obtain whole blood and blood components from areas of the United States without active virus transmission until a blood donor screening test for Zika virus became available to ensure the safety of their blood supply. Until blood donor screening tests for Zika virus became available, HHS arranged for and funded shipments of blood products from the continental United States to Puerto Rico to ensure an adequate supply of safe blood for its residents during this interim period. Concomitantly, FDA worked closely with the test kit developers in a highly accelerated time frame to make available the first investigational test for blood screening in March 2016. The availability of this investigational test, which has been in use in Puerto Rico since early April 2016, enabled blood establishments to resume safe blood collection in areas with active Zika virus transmission. A second investigational blood screening test was made available in June 2016. Together, these tests enabled blood donor screening to be put in place across the United States where active Zika virus transmission was established as well as in areas where local virus transmission was anticipated, helping to maintain an adequate and safe blood supply.

In August 2016, after careful consideration of the evolving scientific and epidemiologic data (including the significant number of travel-associated cases of Zika across the continental US), consultation with other public health agencies, and taking into consideration the potential serious health consequences of Zika virus infection to pregnant women and children born to women exposed to Zika virus during pregnancy, FDA issued updated guidance recommending that all states and U.S. territories screen blood with an approved investigational blood screening test. The guidance recommended a staggered implementation of blood screening across the nation, with immediate implementation in states and territories with one or more locally-acquired mosquito-borne cases of Zika virus, implementation within four weeks in states with proximity to areas with locally-acquired Zika virus cases or other epidemiological linkages to Zika virus (such as a high number of travel-associated Zika cases), and implementation within 12 weeks in all other states and territories.

FDA worked with blood collection establishments to facilitate implementation of the revised guidance across the U.S. and its territories. As of May 2, 2017, 376 presumptive viremic blood donations have been prevented from entering the blood supply in the United States and its territories.[8]

FDA is continuing to monitor the evolving scientific and epidemiologic data on Zika virus and will update its guidance for blood donor testing as necessary based on additional information that may become available that would support reassessing the blood donor testing situation while adequately protecting the blood supply.

[8] CDC Zika Virus Case Counts in the US; https://www.cdc.gov/zika/geo/united-states.html

Zika virus also poses a risk for transmission by human cells, tissues, and cellular and tissue-based products (HCT/Ps) such as corneas, bone, skin, heart valves, and semen used for medical, surgical, or reproductive procedures. Because of this risk, FDA issued guidance in February 2016 recommending that donors of HCT/Ps be considered ineligible if they were diagnosed with Zika virus infection, were in an area with active Zika virus transmission, or had sex with a male with either of those risk factors, within the past six months. FDA is continuing to assess the evolving scientific and epidemiologic data on Zika virus as well as supporting research to help better understand the persistence of Zika virus in cells and tissues, and will update its guidance if necessary to better reduce the risk of Zika virus transmission through HCT/Ps used for medical, surgical, or reproductive procedures.

CONCLUSION

FDA is fully committed to remaining highly responsive and adaptive to the complex range of issues the Zika virus outbreak has presented and will continue to present. Developing the medical products necessary to help bring this outbreak under control is highly complex and will require a sustained effort. Close cooperation and collaboration within FDA, within the U.S. Government, with our international partners, and with product developers is essential to help facilitate the development and availability of medical products to respond to Zika virus as quickly as possible. FDA is wholly prepared to leverage its authorities to the fullest extent practicable to help accelerate the development and availability of safe and effective products with the potential to help mitigate the Zika virus outbreak as quickly as the science will allow.

Thank you. I am happy to answer your questions.

Mr. MURPHY. Thank you, Dr. Borio.
Dr. Fauci you're recognized for 5 minutes.

STATEMENT OF ANTHONY S. FAUCI

Dr. FAUCI. Mr. Chairman, Ranking Member DeGette, Vice Chairman Griffith, members of the committee, thank you for giving me the opportunity to present to you today in a few minutes the role of the NIH research endeavor in addressing the Zika outbreak. I have some visuals that I'll show if we can get them up.

As you know, I have testified about Zika before this committee before, and what I outlined for you was that the NIH's responsibility ranges from the fundamental basic research, clinical research, expansion of research capacity with the ultimate goal in mind to develop the countermeasures that we have been discussing thus far in the form of diagnostics, therapeutics, and vaccines.

With regard to diagnostics, the CDC, as you had mentioned and that Dr. Petersen responded, is primarily responsible for on-the-ground development rapidly of diagnostics that could address this outbreak. However, the NIH's role in that is to try and develop a pipeline of rapid, specific, low-cost diagnostic tools that are delineated on this slide.

[Slide shown.]

They're divided into a few subgroups. The first are molecular tests to detect the presence of the virus itself in a highly sensitive and specific manner. The second are serological tests, which are the most problematic, namely to detect the immune response of someone who has already been infected and to distinguish that immune response to infections to other flaviviruses, such as dengue. And, third, research resources, namely to make reagents and viral strains available to our collaborators throughout the world.

[Slide shown.]

In addition, we're responsible for clinical research. I will give you one example of that, and that has to do with the Zika in Infants and Pregnancy, or ZIP, study in which we are performing in collaboration with the Fiocruz Institute in Brazil.

[Slide shown.]

It is a prospective cohort study observational of 10,000 pregnant women, following them for the incidence of Zika infection, following their pregnancies to determine the incidence of involvement of the fetus with congenital abnormalities, and then following birth to follow the infants for at least 1 year of age.

[Slide shown.]

However, probably the most important and impactful of what we do is the development of a vaccine.

[Slide shown.]

Now, this slide shows five candidate vaccines that are in various levels of development for Zika. The first one that is on the slide is the DNA vaccine. I want to caution the committee that just because something is temporally ahead of something else in development doesn't necessarily mean it is going to ultimately turn out to be the best vaccine. But we have been fortunate because we have been able to rapidly put several of these into trial, and I want to just mention one of these for the purposes of the discussion this morning. And that is the DNA vaccine.

[Slide shown.]

This is a vaccine that is a 21st century version of vaccinology; namely, we no longer isolate the virus, grow it and activate it or attenuate it, but we use molecular biological techniques.

On this slide is shown how a DNA vaccine works. You get a circular piece of DNA, which is referred to as a plasmid. You insert a gene of a particular protein that you want to make an immune response to, and you then inject that into an individual, and then what happens is that, in response, a virus-like particle is formed, and the body makes a good immune response.

[Slide shown.]

On March 2nd of 2016, I testified before this committee that we were still in animal model, and I said that we would get into a human phase 1 trial very likely by the fall of 2016. And, in fact, we did in September and then again in December, showing that the vaccine was safe, and it induced the kind of response that you would at least predict would be protective.

We also said we hoped to get into a phase 2 trial by the first quarter of 2017.

[Slide shown.]

And, in fact, at the end of March of this year, we actually initiated a phase 2 trial, first in Texas and Puerto Rico, and then, in the next few months, we're going to advance this into the countries shown by the red dots on the slide. We have a flexible capability so that, if there are outbreaks in one country more than the other, we'll be able to divert the resources to be able to get the vaccine deployed in an area where there is an outbreak.

Now there's no guarantee that this is going to be effective or that there are going to be enough cases to at least prove that it is effective, but we are at least on time in our endeavor, and I would hope that, as we follow up on this in the coming year or so, we will be able to come back to this committee and say that we do, in fact, have a safe and effective vaccine.

I'll stop there, Mr. Chairman, and be happy to answer questions later. Thank you.

[The prepared statement and slide presentation of Dr. Fauci follow:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Research Conducted and Supported by the National Institutes of Health (NIH) in Addressing Zika Virus Disease

Testimony before the

House Committee on Energy and Commerce

Subcommittee on Oversight and Investigations

Anthony S. Fauci, M.D.

Director

National Institute of Allergy and Infectious Diseases

National Institutes of Health

May 23, 2017

Mr. Chairman, Ranking Member DeGette, and Members of the Subcommittee:

Thank you for the opportunity to discuss the ongoing National Institutes of Health (NIH) research response to Zika virus. I direct the National Institute of Allergy and Infectious Diseases (NIAID), the lead NIH institute for conducting and supporting research on emerging and re-emerging infectious diseases that pose threats to public health. NIAID funds a comprehensive research portfolio, from basic studies of the mechanisms of disease, to applied and clinical research focused on developing interventions such as diagnostics, therapeutics, and vaccines. We have a dual mandate to support research on established disease threats and to respond rapidly to newly emerging and re-emerging infectious diseases.

Emerging and re-emerging disease threats are perpetual challenges, in part due to the inherent capacity of microbial pathogens to evolve rapidly and adapt to new ecological niches. NIAID anticipates and responds to these threats by leveraging fundamental, basic research; mobilizing domestic and international research infrastructure; and partnering with governments, non-governmental and multilateral organizations, academia, and industry, both nationally and internationally.

I am pleased to be able to discuss with you our research efforts to protect the American people from Zika virus.

OVERVIEW OF ZIKA VIRUS

Zika virus is a flavivirus. These viruses typically are transmitted by mosquitoes or ticks and often can spread quickly to new geographic locations due to the abundance of these vectors. Other well-known flaviviruses include dengue virus and yellow fever virus; like Zika, these viruses are transmitted by *Aedes* mosquitoes. Zika virus, first identified in monkeys in Uganda in

1947, is endemic to Africa and Southeast Asia; however, it recently has spread to other parts of the world. An unprecedented Zika outbreak began in Brazil in May 2015 and has spread throughout South and Central America and into the United States. Widespread local transmission has occurred in U.S. territories including Puerto Rico, and limited local transmission has occurred in areas of Florida and Texas. Although recent Zika case reports in the Americas have decreased from the unprecedented spread of the virus in 2015 and 2016, continued transmission of Zika virus to a greater or lesser degree is expected throughout the western hemisphere.

While infections caused by Zika virus are usually asymptomatic, about 20 percent of infected individuals experience mild clinical symptoms such as fever, rash, muscle and joint pain, and conjunctivitis (red eyes). Increases in cases of Guillain-Barré Syndrome, a rare, acute, immune-mediated peripheral nerve disease that leads to weakness, sometimes paralysis, and infrequently, respiratory failure and death, also have been noted in association with Zika outbreaks in Brazil and elsewhere. Of most concern, the recent outbreaks of Zika virus disease have coincided with a marked increase in the number of infants born with microcephaly, a birth defect characterized by an abnormally small head resulting from an underdeveloped and/or damaged brain. Recent studies have conclusively shown that Zika virus causes microcephaly in infants, as well as an array of congenital abnormalities such as eye defects, hearing loss, impaired growth, seizures, difficulty moving limbs, and other complications known collectively as congenital Zika syndrome. Although it has been established that Zika infection during pregnancy can cause congenital Zika syndrome in the infant, further research is needed to better understand the disease and how to prevent it. Currently, no FDA-licensed vaccines or specific therapeutics are available to prevent or treat Zika virus disease. Improved diagnostic tests also

are needed as Zika virus infection can be difficult to diagnose and distinguish clinically from other mosquito-borne infections, such as dengue, West Nile, and chikungunya.

DEVELOPING COUNTERMEASURES TO COMBAT ZIKA VIRUS

NIAID has responded to the Zika epidemic by accelerating ongoing flavivirus research efforts to speed the development of biomedical tools that could help control current and future outbreaks of Zika virus.

Vaccines

A safe and effective Zika vaccine would be an invaluable tool to help stop the spread of infection and prevent future outbreaks. NIAID is developing and investigating multiple Zika vaccine candidates, including vaccines based on technologies that have shown promise against other flaviviruses. The NIAID Vaccine Research Center (VRC) has developed a candidate DNA-based Zika vaccine akin to a West Nile virus vaccine that we previously developed. The DNA-based Zika vaccine candidate entered a Phase 1 clinical trial in 2016, and initial study results indicate that the vaccine is safe and induces an immune response in the range that would predict that it would protect against Zika virus. NIAID launched a multi-site Phase 2a/2b clinical trial of this vaccine in March 2017 that aims to enroll at least 2,490 healthy participants in various sites in the Americas, including the continental United States and Puerto Rico, Brazil, Peru, Costa Rica, Panama, and Mexico. The trial will further evaluate whether the experimental vaccine is safe and able to stimulate an adequate immune response, and importantly whether it can prevent disease in areas with ongoing mosquito-borne Zika transmission.

NIAID scientists also are developing live-attenuated Zika vaccine candidates using an approach similar to that taken with an experimental vaccine against the closely related dengue virus. This vaccine candidate will enter an NIAID Phase 1 trial in late 2017. Another version of

this approach, an experimental vaccine designed to protect against Zika and all four circulating strains of dengue virus, is scheduled to enter clinical testing by 2018. NIAID is working with academic partners in Brazil to plan later-stage trials of this combination vaccine referred to as a chimeric vaccine.

NIAID also is collaborating with the Biomedical Advanced Research and Development Authority (BARDA) and the Walter Reed Army Institute of Research (WRAIR) to evaluate a Zika purified inactivated vaccine (ZPIV) candidate. Multiple Phase 1 clinical trials of ZPIV began in November 2016 in several U.S. sites.

NIAID-supported researchers also are evaluating investigational mRNA vaccines, which are broadly similar to DNA vaccines. The NIAID VRC is working with academic and industry partners to evaluate various mRNA vaccine technologies to identify potential candidates for further development. These include an investigational vaccine under development by the NIAID VRC and a pharmaceutical company that may enter clinical trials in late 2017.

NIAID grantees also are in the early stages of developing a Zika virus vaccine candidate based on a recombinant vesicular stomatitis virus – the same animal virus used successfully to create an investigational Ebola vaccine. This Zika vaccine construct will be evaluated in tissue culture and animal models. NIAID is supporting diverse early-stage Zika vaccine strategies to maximize our chances of success in rapidly reaching the goal of a licensed vaccine.

While these multiple approaches are promising, it is important to realize that the development of investigational vaccines and the clinical testing required to establish their safety and effectiveness take time. The pace of these trials in reaching a conclusion will depend on both the inherent effectiveness of the vaccine and the amount of Zika virus transmission near clinical trial sites. If a Zika outbreak occurs during the phase 2a/2b vaccine trial, it is conceivable that we

will have an indication of whether the vaccine works within 1 to 1.5 years. However, with the recent decline in Zika cases across the Americas, Zika vaccine clinical trials may require more time to discern whether the vaccine candidates are successful in preventing Zika virus infection. While we have begun clinical testing of several Zika vaccine candidates, a safe, effective, and fully licensed Zika vaccine likely will not be available for several years.

Therapeutics

NIAID has accelerated its program originally designed to screen for antiviral drugs with activity against viruses in the flavivirus family, including dengue, West Nile, yellow fever, and Japanese encephalitis viruses, as well as the closely related hepatitis C virus. NIAID has enhanced these efforts by developing an assay to test compounds for antiviral activity against Zika virus, and has made this test readily available to the broader research community. As of April 30, 2017, NIAID has tested 679 antiviral molecules and identified 39 compounds with high or moderate activity against Zika virus. Promising drug candidates identified by this assay are being further tested in animal models of Zika virus infection developed with NIAID support. For example, NIAID evaluated BCX4430, a broad-spectrum antiviral drug originally developed by a pharmaceutical company as a candidate therapeutic for Ebola and Marburg viruses, and found that the drug protected mice and non-human primates from Zika virus.

NIAID-supported researchers also have identified a human antibody, ZIKV-117, that neutralizes multiple strains of the Zika virus. ZIKV-117 reduces levels of the virus in reproductive tissues and decreases fetal disease in a pregnant mouse model of Zika infection, suggesting that such broadly neutralizing Zika antibodies could be used to treat or prevent Zika virus infection in humans.

Diagnostics

Accurate diagnostic tests are needed to distinguish Zika virus infection from other flavivirus infections and to identify women who have been infected with Zika virus during pregnancy and may be at risk of having an infant with fetal complications. Currently, molecular diagnostic tests for viral RNA can detect Zika virus during the acute phase of infection and for a limited period after the onset of symptoms. After this limited period, prior infection can be detected by testing for the presence of antibodies against Zika virus. However, assays for Zika antibodies also may detect or cross-react with antibodies against other flaviviruses, particularly dengue virus. For this reason, a positive antibody test does not definitively confirm prior Zika virus infection, particularly in geographic areas with ongoing dengue virus infection. In cases of possible co-infection or prior infection with dengue and other related viruses, separate confirmatory testing is required. This is a particular concern in South America, where people have a high level of exposure to other mosquito-borne viruses, especially dengue and chikungunya.

NIAID is facilitating the development of improved Zika virus diagnostic tests through support for NIAID investigators and grantees working to generate antibodies and recombinant protein antigens that can be used to distinguish between Zika virus and dengue virus. Studies also are underway to create new diagnostic methods that simultaneously measure antibody responses to several flaviviruses to clearly distinguish which virus caused a recent infection. In addition, NIAID grantees are working to identify unique biosignatures for Zika infection that could form the basis of other rapid diagnostic tests.

IMPROVING UNDERSTANDING OF ZIKA VIRUS TRANSMISSION

NIAID conducts and supports research on the natural history and transmission of Zika virus. These studies will increase our understanding of the effects of Zika virus during pregnancy and help identify strategies to limit mosquito-borne transmission of the virus.

Natural History

NIAID is partnering with the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the National Institute of Environmental Health Sciences, and the Brazilian research institute Fiocruz to study the link between Zika infection and adverse outcomes such as the congenital Zika syndrome. This study, Zika in Infants and Pregnancy (ZIP), is a multi-center, international, prospective study of 10,000 women in Zika-affected regions. Enrollment of women early in their pregnancy is ongoing, and their children will be followed for at least one year after birth. The information gained from this study will help improve our understanding of congenital Zika syndrome, enhance care for pregnant women and their infants, and guide interventions for affected children.

Vector Control

For many years, NIAID has supported extensive research on the biology of mosquitoes to help develop tools to limit the spread of deadly mosquito-borne diseases such as dengue and malaria. This research informs vector control strategies to reduce mosquito bites or limit mosquito populations. In the Americas, Zika virus is transmitted primarily by *Aedes aegypti* mosquitoes, and vector control or other methods to prevent exposure to these mosquitoes are currently the only ways to prevent Zika infection.

NIAID is supporting vector competence studies to test various mosquito species for their ability to carry and transmit Zika virus, as well as research to prevent resistance of mosquitoes to

insecticides and identify the emergence of resistance early so it can be managed appropriately. Understanding the specific mosquito species involved in Zika outbreaks and which insecticides may be effective against them will aid current vector control efforts. In addition, NIAID is supporting innovative vector control research, including evaluation of novel repellents, mosquito traps, and the use of bacterial symbionts to affect mosquito biology and reproduction.

CONCLUSION

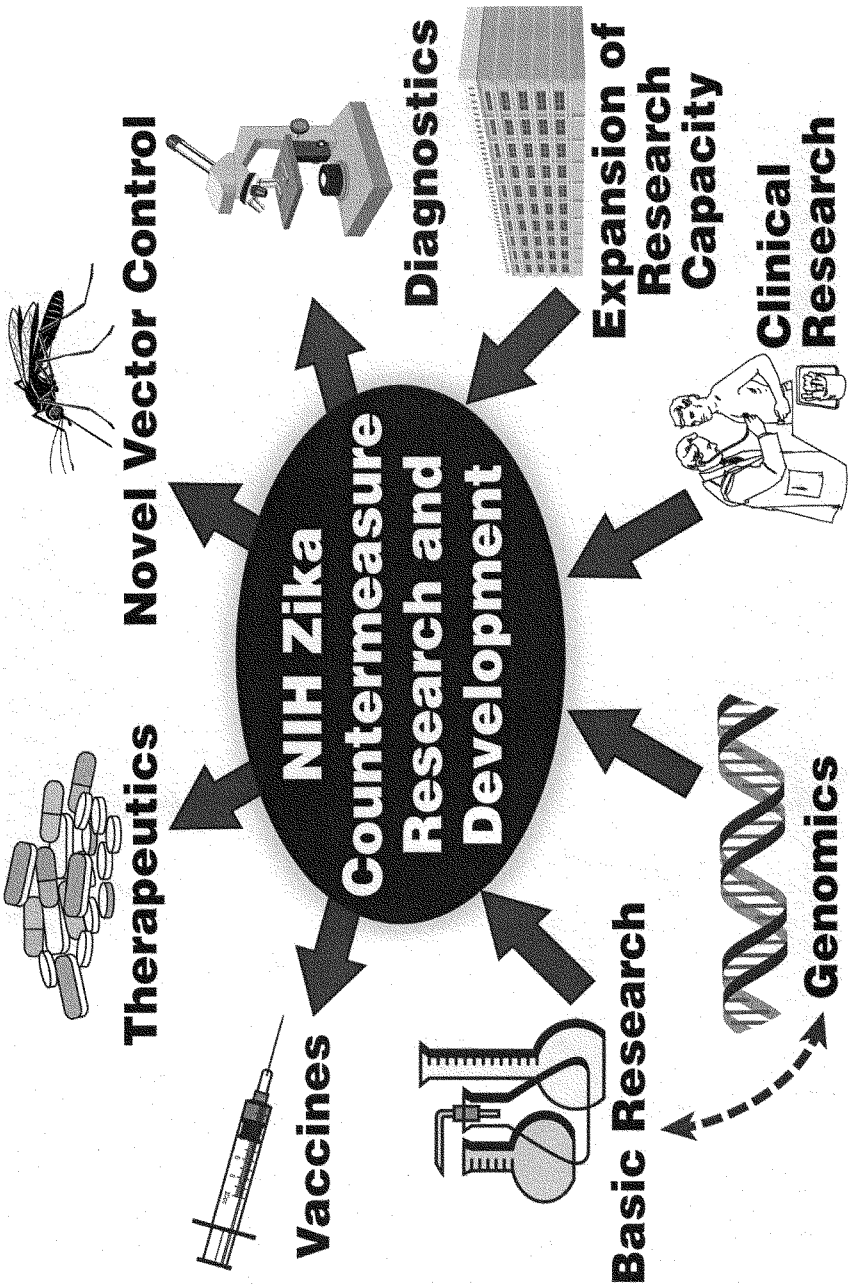
NIH is committed to robust collaborations with partners across the U.S. government, academia, and industry to further advance research to address Zika virus infection. As part of its mission to respond rapidly to emerging and re-emerging infectious diseases globally, NIAID is elucidating the biology of Zika virus and developing tools to diagnose, treat, and prevent disease caused by this virus. As a high priority, NIAID will continue to pursue the development of safe and effective vaccines and therapeutics against Zika virus. All of these efforts will expand our understanding of this current public health threat, improve our preparedness for the next emerging infectious disease outbreak, and continue to provide evidence-based strategies to promote public health.

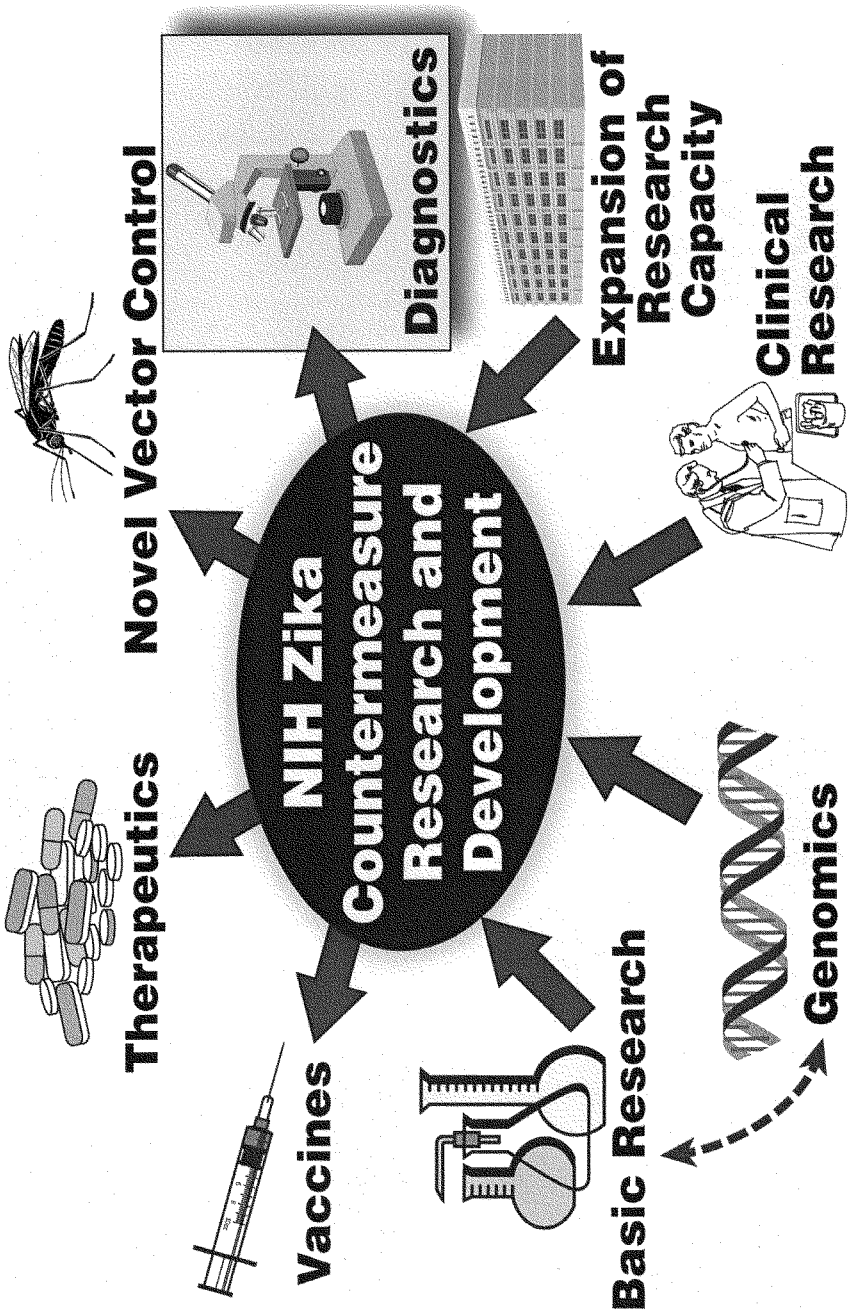
Hearing of the House Energy and Commerce, Oversight and Investigations Subcommittee

The Role of the National Institutes of Health in Research Addressing Zika Virus

Anthony S. Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
May 23, 2017

National Institute of Allergy and Infectious Diseases


NIH Zika Countermeasure Research and Development
Novel Vector Control
Diagnostics
Expansion of Research Capacity
Clinical Research
Genomics
Basic Research
Vaccines
Therapeutics


NIH Zika Countermeasure Research and Development
Novel Vector Control
Diagnostics
Expansion of Research Capacity
Clinical Research
Genomics
Basic Research
Vaccines
Therapeutics

NIAID Zika Diagnostics Research

Goal: Development of rapid, specific, low-cost diagnostic tools, e.g.

- **Molecular tests**
  - **To detect the presence of the virus itself in a highly sensitive and specific manner**
- **Serological tests**
  - **To detect the immune response (usually antibody) to the virus and distinguish from responses to other flaviviruses**
- **Research resources**
  - **Reagents and viral strains made available to collaborators**

Therapeutics
Novel Vector Control
Vaccines
NIH Zika Countermeasure Research and Development
Diagnostics
Basic Research
Expansion of Research Capacity
Genomics
Clinical Research

Zika in Infants and Pregnancy (ZIP) Study

- Sponsored by NIH and Oswaldo Cruz Foundation (Fiocruz) of Brazil
- Prospective cohort study of 10,000 pregnant women
- Following women for incidence of Zika infection
- Following infants through at least one year of age
- Key endpoints: pregnancy outcomes, congenital anomalies, other developmental abnormalities

Therapeutics
Novel Vector Control
Vaccines
NIH Zika Countermeasure Research and Development
Diagnostics
Basic Research
Expansion of Research Capacity
Genomics
Clinical Research

NIH Zika Vaccine Candidates

DNA vaccine (NIAID VRC)

- **Zika purified inactivated vaccine** (WRAIR/NIAID/BARDA and Sanofi Pasteur)
- **Live-attenuated Zika/dengue chimeric virus** (NIAID intramural/Butantan)

mRNA vaccine candidate (NIAID VRC, GSK)

- **Vesicular Stomatitis Virus vectored vaccine** (NIAID extramural)

NIH Zika Vaccine Candidates

DNA vaccine (NIAID VRC)

- **Zika purified inactivated vaccine** (WRAIR/NIAID/BARDA and Sanofi Pasteur)
- **Live-attenuated Zika/dengue chimeric virus** (NIAID intramural/Butantan)

mRNA vaccine candidate (NIAID VRC, GSK)

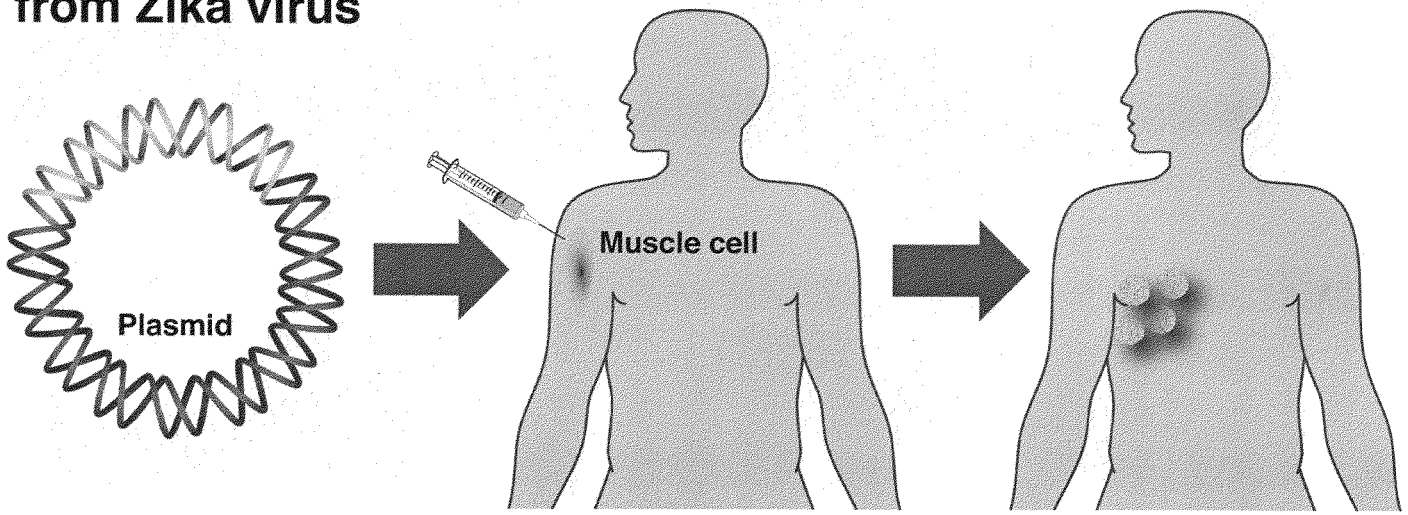
- **Vesicular Stomatitis Virus vectored vaccine** (NIAID extramural)

DNA Vaccine Approach

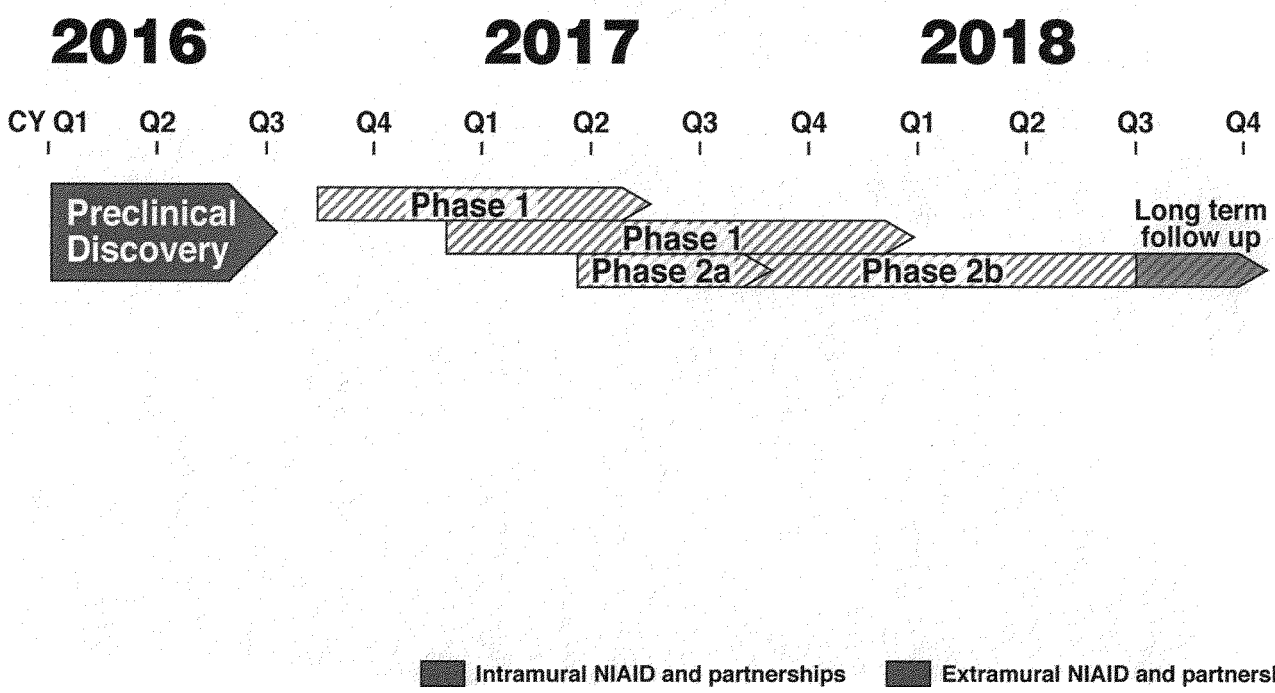
Gene encoding surface protein from Zika virus

Inject DNA containing Zika gene

Body's cells produce virus-like particles, the basis of the vaccine



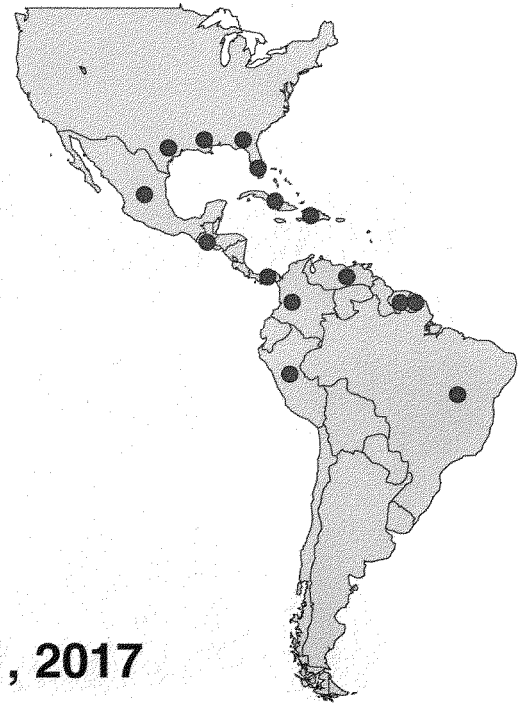
Zika DNA Vaccine Timeline



Phase 2/2b: ZIKV DNA Vaccine Candidate

- VRC 705: A Phase 2/2b, Randomized, Placebo-Controlled Trial to Evaluate the Safety and Immunogenicity of a Zika Virus DNA Vaccine, VRC-ZKADNA085-00-VP

- 30+ sites in the US, Caribbean, Central and South America



Launched March 31, 2017

Mr. MURPHY. Thank you, Dr. Fauci.
Dr. Bright, you're recognized for 5 minutes.

STATEMENT OF RICK A. BRIGHT

Dr. BRIGHT. Good morning, Chairman Murphy, Ranking Member DeGette, and distinguished members of the subcommittee. I'm Dr. Rick Bright, the Director of the Biomedical Advanced Research and Development Authority, otherwise known as BARDA. I'm also the Deputy Assistant Secretary for Preparedness and Response in the Office of the Assistant Secretary for Preparedness and Response, or the ASPR, within the U.S. Department of Health and Human Services.

I appreciate the opportunity to speak with you today. This is the first opportunity I have had to testify since being named the BARDA Director last November.

As a component of ASPR, BARDA was established to aid in securing our Nation from chemical, biological, radiological and nuclear threats as well as from pandemic influenza and other emerging infectious diseases.

BARDA supports the transition of medical countermeasures, such as vaccines, drugs, and diagnostics, from research stages through advanced development toward consideration for approval by the FDA and often into the Strategic National Stockpile. Our mission is accomplished through the successful public-private partnerships with industry to share the risk, improve efficiency, and accelerate development, all while sustaining the marketplace for countermeasures that are vital for our national security.

BARDA also collaborates and coordinates very closely with our Federal colleagues through the participation in the Public Health Emergency Medical Countermeasures Enterprise, which is chaired by the HHS ASPR. To support the overall HHS response to Zika, BARDA has established three goals to address medical countermeasure gaps: first, the prevention of Zika virus infection through the development of safe and effective vaccines; second, for the rapid detection of infection through the development of diagnostics; and, third, to ensure a safe blood supply by the development of screening tests for Zika and technologies that will inactivate pathogens in donated blood products.

For diagnostics, our goal is to stimulate and accelerate the development of rapid and accurate serological tests. BARDA has partnered with five companies to support these tests. Some of these tests are laboratory based, and some of these tests are for point-of-care use.

BARDA is also supporting the development of two tests that are now being used under an FDA investigational new drug protocol to screen Zika virus in donated blood. BARDA is also supporting the development of four Zika vaccine candidates. One candidate began as a collaboration between BARDA, the U.S. Department of Defense, and NIAID. And it is currently in multiple clinical trials. This candidate has now transitioned to an industry partner for further development.

To introduce additional innovation into this outbreak, we are also supporting the development of a vaccine candidate that is based on a novel messenger RNA platform that is now in clinical

trials. This is a new vaccine platform that has potential to develop and produce vaccines rapidly. This is essential for an effective response to emerging threats.

Funding from Congress has been critical for our response to Zika. However, additional support will be needed to continue our progress. There is great value in keeping multiple candidates in the pipeline to increase the chance of success. Looking ahead, also having a Federal emergency response fund would contribute to a rapid medical countermeasure response for future public health threats.

BARDA and ASPR are committed to using innovative technologies and innovative contractual tools to accomplish our mission. A nimble and flexible, yet consistent and transparent approach is critical to successful public-private partnerships, not only to address the early valley of death, but also to address challenges of market entry and sustainability that our industry partners face when products are approved. It is important to sustain capacity, capability, and partnerships with the private sector to be ready and able to respond when we confront threats to our national security and public health.

Mr. Chairman, ASPR and BARDA are working with HHS colleagues, our interagency colleagues, and our private sector partners to prepare our Nation for range of national security and public health threats. Medical countermeasure development is a long, complicated, and a high-risk process. BARDA is greatly appreciative of the resources and authorities that Congress has provided to us to accomplish its mission. I look forward to working with members of this subcommittee and your congressional colleagues. I'm grateful for the opportunity to address you today, and I'm happy to take your questions.

[The prepared statement of Dr. Bright follows:]

Written Testimony
House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations

Zika Virus Outbreak and Response

Statement of

Rick A. Bright, PhD

Deputy Assistant Secretary for Preparedness and Response and
Director of the Biomedical Advanced Research Development Authority
Office of the Assistant Secretary for Preparedness and Response
U.S. Department of Health and Human Services

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

For Release on Delivery
Expected at 10:00 a.m.
May 23, 2017

Good morning, Chairman Murphy, Ranking Member DeGette, and distinguished members of the House Energy and Commerce Subcommittee on Oversight and Investigations. I am Dr. Rick Bright, Director of the Biomedical Advanced Research and Development Authority (BARDA) and Deputy Assistant Secretary for Preparedness and Response in the Office of the Assistant Secretary for Preparedness and Response (ASPR). I appreciate the opportunity to speak with you today, the first opportunity I have had to testify since being named the BARDA director in November 2016. After spending a number of years developing influenza vaccines and therapeutics at the Centers for Disease Control and Prevention (CDC) and working in senior management positions in the biopharmaceutical industry, I joined BARDA in 2010. Before assuming the director role, I served in various roles in BARDA that focused on the development of vaccines, therapeutics, and diagnostics and as the director of the Division of Influenza and Emerging Infectious Diseases. My experience in medical countermeasure development in government, non-government organizations, and industry provide a firm foundation for my role as the BARDA director.

As a component of ASPR, BARDA was established in 2006 under the Pandemic and All-Hazards Preparedness Act (PAHPA). BARDA has a role in securing our nation from chemical, biological, radiological, nuclear, pandemic influenza and emerging infectious disease threats by supporting the transition of medical countermeasure candidates from early development across the "Valley of Death" and into advanced research and development towards an application for approval by the Food and Drug Administration (FDA). BARDA executes this mission by providing push and pull incentives to stimulate a robust pipeline of medical countermeasures for these threats and by forming public-private partnerships with industry to reduce risk, improve

efficiency and sustain a marketplace for development and procurement of these countermeasures. BARDA is comprised of a staff of highly skilled, technical experts, many of whom have decades of experience in the pharmaceutical industry. Since 2006, we have established partnerships with over 100 pharmaceutical and biotechnology companies and more than 25 academic and other institutions.

BARDA has established an array of specialized core services to support medical countermeasure advanced development efforts. These services facilitate access to experienced subject matter experts in a variety of disciplines germane to product development (such as clinical trial strategy and execution, regulatory sciences, quality control and quality assurance, production process engineering). BARDA also provides leadership by collaborating with HHS partners in animal model development and preclinical laboratories, by maintaining a clinical studies network (a network of companies to formulate and fill vaccines into final containers), and through BARDA's Centers for Innovation in Advanced Development and Manufacturing (CIADM). These national assets, known collectively as BARDA's National Medical Countermeasures Response Infrastructure, support BARDA's core mission of promoting biodefense product development and enhance BARDA's response capability. These capabilities are currently being leveraged for the Zika response in a similar way as they supported the response to Ebola and pandemic influenza.

BARDA collaborates strategically with its U.S. Government colleagues around medical countermeasure development through participation in the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE). The PHEMCE, chaired by the ASPR, is a standing

virtual enterprise that coordinates the entire life cycle associated with the development and procurement of medical countermeasures for these emergency public health threats. It engages all of the key Federal departments and agencies that develop, procure, or distribute these important medical countermeasures and was created to improve coordination and collaboration within the Department and with our external stakeholders including nonprofits, other Federal departments, the private sector, and the international community.

Against this backdrop and overarching objectives for Zika response, BARDA established four strategic goals to address the medical countermeasure needs for the domestic and global Zika response. These are prevention of Zika virus infection through safe and effective vaccines; detection of acute and previous Zika virus infections through rapid diagnostics; ensuring a safe blood supply from Zika virus through screening and virus inactivation; and activation of our National Medical Countermeasure Response Infrastructure to assist in the development of medical countermeasures for Zika.

With funds provided from Congress in fiscal years 2016 and 2017, we have contributed to the overall HHS response to Zika by supporting the development of new Zika-specific vaccine candidates; vaccine platform technologies that will be able to address multiple emerging infectious diseases; development of rapid serological diagnostics to determine whether someone, including pregnant women and their male partners, has been infected recently with the Zika virus; tests to screen the blood supply for presence of Zika virus; and pathogen reduction technologies that will inactivate Zika virus and other pathogens in donated blood to reduce the risk of Zika virus transmission through blood transfusions.

In February 2016, BARDA participated, with its U.S. Government colleagues, in drafting aligned strategies for development of vaccines and diagnostics for Zika. For diagnostics, our goal was to stimulate and accelerate the development of diagnostic tests to speed the availability of results and inform people of their Zika virus exposure. We rapidly modified our Broad Agency Announcement to allow us to receive proposals to address this requirement. The response from industry was robust. Compiling funds received from repurposed Ebola appropriations with other sources of funding, BARDA awarded four contracts during the summer of 2016 for the development of Zika diagnostics that would determine whether people have had recent exposure to Zika. Industry partners currently supported by BARDA include InBios and DiaSorin to develop a laboratory-based serological test to detect IgM antibodies (indicating recent infection), and OraSure and Chembio to develop a point-of-care diagnostic test that would allow for rapid results for the clinician and patient. Two of these companies have received Emergency Use Authorizations from the FDA for their Zika test: InBios for their ZIKV Detect IgM Capture ELISA and DiaSorin for their LIAISON XL Zika Capture IgM Assay. In addition, BARDA, in close coordination with CDC, addressed a critical barrier for diagnostic developers by collecting blood specimens that contained Zika virus to create well-characterized panels for use in assessing how well the tests perform.

BARDA's role in addressing the blood supply shortage in Puerto Rico is another notable success story. On February 16, 2016, the FDA issued Zika-related blood donor guidance recommending, among other things, that areas with active Zika virus transmission, like Puerto Rico, obtain whole blood and blood components for transfusion from areas of the United States without active Zika virus transmission unless a blood donor screening test for Zika virus is used. Additionally,

the guidance recommended the deferral of individuals from donating blood if they have been to areas with active transmission such as Puerto Rico, potentially have been exposed to Zika, or have had a confirmed Zika virus infection. Because there were no blood donor screening tests available for Zika virus at that time, BARDA worked with CDC, FDA, and the Office of the Assistant Secretary of Health (OASH) to define requirements, conduct market research, obtain legal advice, and award a contract to transport blood products from the U.S. mainland to Puerto Rico to avoid a blood product shortage until a blood donor screening test became available. With BARDA's financial support, Roche Molecular Systems was able to test blood donations from Puerto Rico starting April 2016 under their FDA approved investigational ZIKV nucleic acid test. This entire process was completed in only six business days after being notified of the impending blood product shortage. This is just one of many examples of progress made possible thanks to our response-based programs and close collaboration with our colleagues across the Department.

BARDA has been working closely with our government and industry partners to identify and develop Zika vaccine candidates. BARDA hosts a carefully designed program, called TechWatch, that invites any individual or company to request a meeting with BARDA through our medicalcountermeasures.gov website. Our TechWatch program serves two primary functions: first to inform and communicate our medical countermeasure requirements to potential industry partners and second, to learn about medical countermeasure candidates that are in development. BARDA has hosted several TechWatch "marathons" to engage with companies that are developing Zika vaccine, therapeutic, and diagnostic candidates. BARDA is able to provide subject matter expertise, advice, and referrals at these engagements. Some of these

meetings lead to the submission of a white paper or proposal to BARDA to consider advanced development support of the specific candidate.

One essential function of BARDA is to work with industry partners to guide product candidates across advanced development towards an application for FDA approval. As it currently stands, many of the Zika vaccine candidates that are supported by BARDA are in the early stages of or making progress towards clinical development. Among these candidates, Sanofi Pasteur, Takeda, and the Instituto Butantan are working on whole virus inactivated vaccine candidates. This is a more traditional, conservative approach to development of a vaccine type that has shown to be successful for other flaviruses, such as the Japanese encephalitis vaccine. This vaccine approach has been used for many vaccines and has a proven track record for safety and immunogenicity. The vaccine being developed by Sanofi Pasteur is an extension of a collaboration that started with the Department of Defense's Walter Reed Army Institute of Research (WRAIR), the National Institute of Allergy and Infectious Diseases (NIAID) and BARDA. Sanofi Pasteur is in the process of licensing this technology from WRAIR. The initial vaccine, developed by WRAIR, is currently in several Phase 1 clinical trials in the United States that are being funded by NIAID and WRAIR. Takeda is also making good progress in the development and production of its Zika vaccine candidate and is planning to start its first Phase 1 clinical trial this fall. The Instituto Butantan, based in Sao Paulo Brazil, has received BARDA's support to develop a Zika vaccine for use in Brazil and other countries. This partnership builds on a past successful collaboration with Butantan on the development and production of influenza vaccines.

BARDA is also working with Moderna to develop a Zika vaccine based upon its novel messenger RNA (mRNA) platform. This is an exciting new vaccine platform that has the potential to rapidly develop and produce vaccines at a large scale—which is essential for response to emerging threats. Moderna recently published encouraging clinical data using this platform for an influenza vaccine candidate and, with BARDA's collaboration, it is currently conducting Phase 1/2 clinical trials that will assess the safety and immunogenicity of its vaccine candidate for Zika. Moderna is also expanding and optimizing its vaccine manufacturing scale to produce vaccine in preparation for later stage clinical studies.

Clinical efficacy trials for Zika vaccine candidates pose an added challenge. One objective of such trials is to collect data to support that a vaccine is safe and effective at preventing infection from Zika virus. However, at this point in time, the Zika virus has already spread through major urban centers in Brazil, throughout Puerto Rico, and other regions in Central America. This means that many people have already been exposed to the Zika virus and are likely already immune to reinfection. In order to conduct large-scale efficacy clinical trials for Zika vaccines, it is important to pre-position clinical sites where we assess that there may still be a significant population naïve to Zika but also where the virus is likely to appear. Thus, it can lead to a chase of the virus around the globe. Our BARDA modelers, in close coordination with CDC and NIH, are working to estimate where Zika may appear next. This work is informing our clinical and regulatory strategies and options to consider as we progress with vaccine development.

The funds that BARDA has received to date have been put to work to accelerate the development of Zika vaccines, diagnostics, and methods to ensure a safe blood supply. While these funds

were instrumental in pushing these candidates into initial clinical trials, additional funding is needed to support Phase 3 clinical trials for the most promising Zika vaccine candidates. At BARDA, we know the value of having multiple candidates in the pipeline to reduce the development risk and increase the chance of getting one or more vaccines to the finish line. With Zika virus, we continue to learn new things about the virus and the disease that it causes almost every week. Now is the time to keep the development pressure strong, to remove any barriers to rapid development and clinical evaluation of these vaccines, and to strive to have a vaccine that can be used to address any outbreak of Zika virus in the near future. Our ultimate goal is to have a vaccine available that will prevent anyone from getting infected with Zika virus. This could have a significant impact on preventing the outcomes we are now seeing from babies born to mothers who have been infected with Zika during pregnancy. BARDA and ASPR are committed to using innovative contractual methods, such as other transactional authorities, while exploring more flexible incentives and financial tools. A nimble and flexible approach is critical to address both the "Valley of Death" between basic research and advanced development, as well as the challenges that our development partners in industry may face when their products are licensed or cleared and enter the market.

The challenges ahead for Zika virus medical countermeasures include those inherent with flaviviruses, an unpredictable virus that could make both clinical development and sustaining an eventual market for countermeasures difficult. The creation of a Federal Emergency Response Fund could enable rapid response to public health outbreaks. Zika is once again a reminder of the challenges we seem to increasingly face in response to emerging diseases. Every day of delay in an emergency response can often be measured by lives lost or a negative impact on our

health or societal stability. Our efforts on Zika virus vaccines and diagnostics have shown once again that the BARDA model is very effective for a rapid medical countermeasure development response.

Mr. Chairman, ASPR and BARDA are working with our HHS and interagency colleagues and our private sector partners to prepare our nation for a range of public health threats. We are making efficient use of the resources Congress has provided and we are making investments and progress as transparent as possible considering proprietary and contractual obligations. This is a long and complicated process, but rest assured, we are up for the challenge. I look forward to working with members of this committee and your Congressional colleagues as HHS continues its response to Zika.

Mr. MURPHY. Thank you.

That is quite a bit of knowledge here. So let me recognize myself for 5 minutes to start this process.

Dr. Fauci, I guess you have been around since 1968, working through about eight Presidents here. So you may have learned a thing or two about this, but I just wonder, how did the pace of this progress on Zika vaccine compare with how quickly vaccines were developed for some of the other viruses?

Dr. FAUCI. Thank you for that question, Mr. Chairman. It actually is the fastest that we have done, because, if you look at the time from either the isolation of a pathogen or sequencing of it—so that you could do a molecular biological approach to the vaccine—Zika is the fastest we have done in history. It is about 3 months from the time that we actually had the sequence that we started putting it into an animal situation. So we really, from the standpoint of the development of a vaccine, which, as you know, with all the things that we have to go through with a vaccine, it takes some time to ultimately get the product, but to hit the ground running from the microbe to the actual vaccine in a preclinical is the quickest we have ever done.

Mr. MURPHY. You also said in your testimony you require more time because of the recent decline in Zika case trials across the Americas. What kind of statistical power do you need here to give you enough numbers on clinical trials? Are you advancing with enough cases here?

Dr. FAUCI. Yes. When you look at the activity that's going on right now, it would probably take a much longer period of time. It is a combination of the statistical power of the end with the amount of time that it would take to get it. So, if you have X number of cases a year, you may take 4 or 5 years to get it. If you get those amount of cases in a particular period of time, like a few months—for example, if there's an outbreak in Puerto Rico as we get into the summer of this coming year in Puerto Rico, we may get enough cases to be able to get an efficacy signal. If there's not, then we may need to wait a longer period of time.

It is a combination of the more effective the vaccine is and the more number of cases, those both come together. If you have you a really effective vaccine and a modest number of cases, then you get your efficacy signal.

Mr. MURPHY. Would this likely then move toward approval for the Emergency Use Authorization of the FDA?

Dr. FAUCI. Well, that really depends, because if you get a good enough signal, you could get Expanded Access; you might not even need to use an Emergency Use Authorization. It really depends on the data and the robustness of the data.

Mr. MURPHY. Let me quickly ask another question here, because we focus a lot on neonatal and prenatal development, et cetera. Any news on studies on men and the impact of Zika virus on men?

Dr. FAUCI. Well, we're continuing to study. As you are I'm sure aware, there was a study that showed, in adult mice, that there's an effect on the testes with oligospermia and testicular atrophy.

Right now, there's no indication that that's the case of an adult male human who gets infected, but we're doing prospective studies now in individuals, and that's related to determining the persist-

ence of Zika in the semen. And you could do two studies. You could see if there's Zika in the semen, and you could also do sperm counts. So we'll be able to know if, in fact, infected individuals have a degree of oligospermia. But that's something that we're looking at in the future.

Mr. MURPHY. I appreciate that.

Dr. Petersen, according to an internal CDC investigative report, the CDC Chief of Diagnostic and Reference Activity in the Arboviral Disease Branch, who had become a whistleblower about the CDC's promotion of the trioplex test for Zika, was moved from that position by DVBD leadership in May 2016. You're the Director of DVBD, and the branch is a part of your division. Why was the CDC expert whistleblower moved out of his position in the middle of the Zika emergency response, and why was he then reinstated as Chief in July of 2016?

Dr. PETERSEN. Thank you for that question. I cannot speak to personnel issues, but I can present a little bit of background about the situation.

There was some discussion among our scientists about the analytic sensitivity of the CDC trioplex test versus a laboratory-developed test known as the monoplex test, and at the time, the trioplex test had actually been EUA approved and was already being distributed to State public health laboratories and laboratories within the laboratory response network. So that test had been distributed already.

An investigation was done into the whistleblower complaint by an independent panel with our Office of Laboratory Safety and Science. And that panel concluded that there was no wrongdoing on the part of CDC. Those results were reviewed by HHS and the Office of General Counsel, which came to the same conclusion.

In the end, we had to make a very rapid decision because there were many women wanting test results. We decided to stay with the trioplex. In the end, it turned out that the trioplex, when tested with a larger panel of samples, was actually an extremely good test, in fact, one of the best out there.

Mr. MURPHY. Thank you. I'm out of time.

Ms. DeGette, you're recognized for 5 minutes.

Ms. DEGETTE. Thank you, Mr. Chairman.

As I said in my opening remarks, I'm really interested both in our position going into the 2017 mosquito and travel season, but also our preparedness in the future.

Dr. Persons, in your audit, you found that agencies like the CDC and FDA face a number of challenges when it came to addressing the Zika threat. One of the challenges is that the Federal Government had insufficient modeling capability for predicting the spread of the Zika virus. Is that correct?

Dr. PERSONS. Yes.

Ms. DEGETTE. And you also found that the CDC and its public health partner agencies faced challenges in establishing and implementing Zika surveillance systems. Is that correct?

Dr. PERSONS. Yes.

Ms. DEGETTE. And, also, Dr. Persons, your audit found that authorized diagnostic tests used for the Zika virus outbreak in the

U.S. varied in both their performance and operational characteristics. Is that right?

Dr. PERSONS. Yes.

Ms. DEGETTE. Now, we're facing an increased array of pandemic threats: Ebola, avian flu, dengue, and now Zika. Although Zika is a unique virus, those challenges that we faced last year suggest the need for better preparedness overall. I'm concerned that what these things I just talked about have grave implications for our overall preparedness posture.

I'm wondering if you can comment briefly about what the broader implications of the challenges on Zika are as they relate to the overall preparedness and where we need to still look at having preparedness for other infectious diseases that might come along.

Dr. PERSONS. Yes, thanks, Ms. DeGette, for the question. As I think our study showed, Zika is a key issue at this point and another case, but it is still one of a type. So it is a pattern, as you all had pointed out. I think what is necessary is a more proactive framework for emerging infectious diseases that will include perhaps the idea of perhaps establishing a case definition earlier on, as soon as you can maybe iterate on that, rather than waiting until things happen here in the U.S. and that has to develop and we have sort of a U.S. stamp on that.

Another thing is just getting data and information as quickly as possible about the accuracy and the limitations of reliable diagnostic tests. It also will be important to have evidence for diagnostic users or practitioners to have that, practitioners would be including scientists as well as clinicians, and certainly, whenever there's a mosquito- or vector-borne disease like this one, I think we're going to need to have more proactive standing infrastructure in terms of dealing with mosquito control.

Ms. DEGETTE. Dr. Petersen, does your agency feel like those are good recommendations and we can use those in the future?

Dr. PETERSEN. Those were very good recommendations. We certainly need a more proactive approach to dealing with mosquito-borne diseases, and the one thing we have learned, with the onset of, incursion of West Nile, then chikungunya, now Zika virus, is that these pathogens are coming to our shores at a more rapid rate than ever before, and we feel that we need to respond and prepare for the unexpected. Nobody would have predicted that Zika virus would be sexually transmitted. Nobody would have predicted any of the factors with that virus.

Ms. DEGETTE. Right. Thank you. You know, last year, Congresswoman DeLauro proposed the creation of an emergency fund that would allocate $5 billion in funds for public health response efforts in advance of disease outbreaks simply because these things are also unpredictable, which would help us from having to scramble at the last minute to find this money.

Dr. Fauci, what do you think about the idea of an emergency fund of this nature?

Dr. FAUCI. I think it's a good idea, and I've actually suggested it myself, as has Tom Frieden, when he was the Director of the CDC. And the reason that we did that is the experience that you alluded to in some of the comments from the committee and that

the President had asked for a certain amount of money in February of 2016, 1.9 billion. And it wasn't until the end of September——

Ms. DEGETTE. Right.

Dr. FAUCI [continuing]. That we got it. And that was really tough.

Ms. DEGETTE. Because the season was almost over by then.

Dr. FAUCI. Yes. And we had to move money from other areas to be able to start our activities. And we moved them from Ebola. We moved them from other things.

Ms. DEGETTE. I remember. I was in those meetings.

Let me just ask you one more question, Dr. Fauci. What does Congress need to do to better help your agency and the other agencies on this panel better prepare for the next infectious disease epidemic?

Dr. FAUCI. Well, I think, as this committee has done in the past—and we are very grateful for that—is that continuing support, of the consistency of our support, because this is a marathon. If you have a sprint for every single outbreak, that's not good. This whole thing is a marathon, and we have to be prepared in a consistent way over the years with consistent support.

Ms. DEGETTE. Over time.

Dr. Bright, you're nodding yes.

Dr. BRIGHT. I absolutely agree. I think it's important that—we've appreciated all the support from Congress, but I think it's important to keep it constant, keep it consistent, keep the process transparent so we can bring innovation to the table to be able to be more proactive for these threats and not less reactive.

Ms. DEGETTE. Thank you.

Thank you, Mr. Chairman.

Mr. MURPHY. Thank you.

We will recognize Mr. Walden, chairman of the committee, for 5 minutes.

Mr. WALDEN. Thank you, Mr. Chairman.

I want to commend our public health agencies for their extensive and very valuable work that you've accomplished during the response to Zika last year. In particular, the pace of Zika virus vaccine research and development has been really impressive, and we've talked about this before, and I congratulate you on that.

Dr. Fauci, when do you think a Zika vaccine will be available for patients? What's your current view of that?

Dr. FAUCI. Thank you for the question, Mr. Walden. But I have to be honest with you: I can't predict that. And the reason you can't predict it, it's going to be based on two factors: one, how inherently good the vaccine is, and how long it takes us to prove how good it is.

So you might have a very good vaccine, and, because of good public health measures or just luck, we don't have a lot of cases of Zika—it may take years before you finally prove statistically that it's good enough for the FDA to approve it. On the other hand, if you have a vaccine that's moderately effective but not really good effective, it still may take longer.

So the best-case scenario from the standpoint of a vaccine, but not from the standpoint of the unfortunate people who suffer from the disease, is that if you have an outbreak over, let's say, the next

season, and you have your vaccine implemented and deployed in place, you may be able to get an efficacy signal sometime, for example, in the beginning or mid of 2018.

And then how good that signal is, the FDA will, in an unbiased way, evaluate that and make a decision. That's the best possible scenario.

Mr. WALDEN. All right. So we're a ways off.

Dr. FAUCI. Right.

Mr. WALDEN. Dr. Bright, I understand there are many candidates for diagnostic tests and vaccines in development today, far more than when we first learned about Zika last year. How do public-private partnerships expedite the development of medical countermeasures?

Dr. BRIGHT. Thank you for your question. It's very important to understand and recognize the contribution of the private sector, especially in responding to a public health emergency. Many of these companies are already focused on other more lucrative products and candidates in development.

And to be able to bring the public and private sectors together for these emergency responses allows us to share the risk of development of these candidates, allows us to share the cost of development of these candidates, and it reduces and mitigates some of the pitfalls that we will face in a traditional, less supportive approach to developing medical countermeasures. So the public-private partnership is a critical component of success.

Mr. WALDEN. All right.

Dr. Petersen, your written statement noted that, and I quote, "Alarmingly, the emergence of mosquito-borne diseases appears to be accelerating," close quote. Why does the CDC believe that the pace of emerging infectious diseases is accelerating? What's behind that?

Dr. PETERSEN. I think there's several causes. One of the major causes is world population growth. We have the growth of mega cities in places where these viruses normally circulate in the tropical world. Combined with increases in travel and trade brings these viruses very rapidly to every corner of the Earth in a very short period of time.

There's other factors that may be involved, such as climate change and other factors. And it's kind of a mixture of factors that's all promoting the emergence of these diseases.

Mr. WALDEN. And in your written statement, you also mention that we need to address the threat of vector-borne diseases systematically rather than episodically. How would the CDC suggest that we address the threat systematically?

Dr. PETERSEN. Well, I think we need to do two things. One is we need to increase our efforts towards innovation and discovery. We need better mosquito control methods, for example. We need better surveillance, et cetera, which will help us with the incursion of any kind of a pathogen, vector-borne pathogen that's coming in.

The other aspect is, is that we need to develop a more national and sustained approach towards vector control and laboratory testing; in other words, a more comprehensive approach towards—a programmatic approach towards dealing with these vector-borne diseases. Improving laboratory diagnostics, improving mosquito

control, improving surveillance, for example. And this will require a sustained effort to rebuild the infrastructure that has been lost in the previous years.

Mr. WALDEN. All right. My time has expired. Thank you all for your testimony and your good counsel.

And I yield back.

Mr. MURPHY. The gentleman yields back.

I recognize Mr. Pallone for 5 minutes.

Mr. PALLONE. Thank you, Mr. Chairman.

It's clear to me that the ongoing Zika outbreak poses a serious threat to the health and well-being of the American public; in particular, pregnant women and infants are especially vulnerable. In the coming months, it will be crucial that pregnant women infected with Zika, as well as infants born with microcephaly, have access to necessary care and services.

So I wanted to ask a couple questions, first with Dr. Petersen. Can you speak to the role that contraceptives and preventive care services play in our efforts to combat the Zika threat?

Dr. PETERSEN. First, I think it's important to keep in mind that about half of the pregnancies in the United States are unplanned, and about two-thirds of the pregnancies in Puerto Rico are unplanned.

Contraceptives and access for women to long-acting reversible contraceptives is one way that women can delay pregnancy, if they wish to. And so some women may choose to delay pregnancy, but it's not the Federal Government's role in advising women to delay pregnancy. But our goal is really to provide women with the most accurate information possible so they and their physicians can make the determination about pregnancy.

Mr. PALLONE. Let me ask Dr. Fauci, can you describe what kind of treatment and longer-term care will be necessary for infants born with microcephaly?

Dr. FAUCI. Well, in the tragic situations with babies who are born with microcephaly, the long-term care is both difficult and highly expensive. There have been estimates that the lifetime care of a microcephalic baby who actually survives could be measured in the millions of dollars.

Babies who are microcephalic and have severe defects very often do not live beyond a certain limited period of time. And during that period of time, the amount of medical care that's required, the amount of time, both emotional and physical, that's invested in the family is extraordinary. So it's a very difficult and tragic situation that's both emotionally difficult and highly expensive.

Mr. PALLONE. Well, unlike other countries, in the United States we're fortunate to have these elite public health agencies, like CDC and NIH, as well as a strong public health infrastructure to prevent outbreaks from becoming full-blown epidemics.

But, Dr. Fauci, why is a strong public health infrastructure in this country often key to avoiding the types of epidemics that we see play out in other parts of the world?

Dr. FAUCI. I'm sorry. I didn't hear the last—why is it——

Mr. PALLONE. Well, in other words, my impression is that because we have such great public health agencies, we're able to prevent Zika outbreaks from becoming full-blown epidemics.

Dr. FAUCI. Right. Yes.

Mr. PALLONE. And that's not necessarily true in the rest of the world. So, you know, if you wanted to just comment on——

Dr. FAUCI. Sure.

Mr. PALLONE [continuing]. How we're able to avoid these epidemics because of our public health infrastructure.

Dr. FAUCI. Well, as infectious diseases and public health officials, as some of us—maybe all of us—at the table are, you'll never be able to prevent an outbreak of a new infection like Zika or Ebola. The trick is to prevent it from becoming an epidemic or a pandemic.

And I think the reason that we do so well is because of just what you've alluded to, Mr. Pallone, that we have in place systems. And I think I can add a tip of the hat to the CDC, because we have, in our Nation, unquestionably the best public health agency in the world by far.

And that's one of the reasons why we have the capability of doing what they do so well, is to identify, to track, and to control. And they've done that with virtually every threatening outbreak that we've had and have done an extraordinary job. And not every country in the world has that capability.

Mr. PALLONE. You know, with this in mind, of course, President Trump has proposed slashing Medicaid by over 800 billion. I believe this would decimate the Medicaid program, which plays a key role in our public health infrastructure. And cutting Medicaid would also further reduce our ability to provide care to those who may need it as a result of Zika, especially pregnant women and children born with microcephaly.

So, Mr. Chairman, you know, again, I think we should be building up our healthcare infrastructure to prepare and respond to Zika. And it's of the utmost importance that we ensure access to the care and services that will be necessary to mitigate this threat.

Dr. Petersen, very quickly, you mentioned contraceptives, but what about preventive care in general in our efforts to combat the Zika threat, not just the contraceptives but the preventive care?

Dr. PETERSEN. Well, first, we're trying to link pregnant women who may have been exposed to the virus to effective care through our Zika Care Connect program, which we funded in a number of States and areas to do.

Again, we think that the best way to deal with Zika is to prevent it. And for that reason, we have issued travel advisories to more than 62 countries, and they're still working—trying to get the right epidemiology to advise women appropriately on what measures they could take to prevent Zika virus, as well as what areas may or may not be safe to travel to to prevent Zika virus infection.

Mr. PALLONE. All right. Thank you.

Thank you, Mr. Chairman.

Mr. MURPHY. Thank you.

I now recognize Mr. Barton for 5 minutes.

Mr. BARTON. Thank you, Mr. Chairman.

I would just point out to my good friend from New Jersey that what we've done with Medicaid is simply slow the rate of growth that we are going to save some money over a 10-year period. We're

not cutting Medicaid. So I just want to set the record straight on that.

We seem to have the top people from all the various medical agencies that are fighting or investigating the Zika virus. Which one of you would be considered the number one official in charge of the research? Somebody answer.

Dr. FAUCI. So I'm not sure what you mean by "in charge of research." The NIH is the primary agency responsible for the research associated with what we're talking about today. The CDC is the agency predominantly responsible for the public health issues of detecting, preventing, and responding.

BARDA is involved in helping the pharmaceutical companies, and all of us develop products that are in intervention, such as diagnostic therapeutics. So there isn't one person that does all of that.

Mr. BARTON. So there's no one in charge.

Dr. FAUCI. Well, there is, because at the Department of Health and Human Services, all of this is under the PHEMCE, which is the Public Health Emergency Medical Countermeasures Enterprise, that involves BARDA, NIH, and CDC, and FDA.

Mr. BARTON. But that person's not here?

Dr. FAUCI. That person's not sitting here, but there is a person that does that.

Mr. BARTON. So there is somebody that is——

Dr. FAUCI. Yes, the Assistant Secretary for public health, for prevention and response.

Mr. BARTON. I'm not trying to be argumentative. It would just seem to be, given the seriousness of this particular virus and the priority that we put upon funding to try to find a vaccine for it, that there would be a unified approach as opposed to all the various groups, all of which have super motives doing their own thing.

Dr. FAUCI. Right. We have the Acting Deputy Assistant Secretary here. So, Rick, do you want to comment?

Dr. BRIGHT. I can add to that, what Dr. Fauci is explaining as well, yes. So the PHEMCE enterprise is chaired by the Assistant Secretary for Preparedness Response, the ASPR.

Right now, we have an acting ASPR, Dr. George Korch. In 2015 and early 2016, our ASPR actually was very proactive in leaning forward and coordinating a meeting across HHS called a disaster leadership group. In early December 2015, we had that first meeting.

In early January of 2016, we had additional meetings that included our partners across the PHEMCE organization, which is outside of the HHS department actually.

Mr. BARTON. Well, this individual—does that individual have the authority to direct funding to the various agencies?

Dr. BRIGHT. That individual has the responsibility for the coordination and alignment of the activities to assure that we are working as efficiently as possible in reducing duplication so the resources are used most efficiently.

Mr. BARTON. I'm not sure I understand that answer.

Dr. FAUCI. The Congress gives us, individually, our resources.

Mr. BARTON. So we——

Dr. FAUCI. Right.

Mr. BARTON [continuing]. Through the authorization and the appropriation process, we fund each agency——

Dr. FAUCI. Yes.

Mr. BARTON [continuing]. And then this individual coordinates?

Dr. FAUCI. Correct.

Mr. BARTON. Well, I guess my bottom-line question is, since you're on the front lines, each of those individuals here, do you believe that we have a unified approach and that money is not being spent in duplicative efforts?

Dr. FAUCI. Yes, I believe we do. In fact, if you look at the Zika response that we've had right from the very beginning, as well as the Ebola response, we actually had the Secretary of HHS involved frequently on, like, weekly conference calls, and in the real hot part of it, multiple per-week conference calls.

But the description that Rick just mentioned is the Assistant Secretary for Preparedness and Response, the ASPR, is the one individual that coordinates what we do—BARDA, FDA, NIH, and CDC—and that's been the case throughout the outbreaks.

Mr. BARTON. OK. I've only got about 30 seconds.

Dr. Fauci, you're certainly the senior person here in terms of service. You didn't really give a direct answer to Chairman Walden's question about when we might expect an effective vaccine. Can you give us a little more definitive, next 2 years, next year, 3 to 5 years? You put some charts up in your testimony. Just give us kind of a ballpark figure. I'm not holding you to the exact date and second, and just generically.

Dr. FAUCI. Yes. A long time ago, a Secretary of HHS gave a ballpark figure for an HIV vaccine, and I think she's still regretting having said that. So I'm not going to give you a time when we'll have a Zika vaccine, except to say that the process for getting to that vaccine is right on time. And I would think it would be measured in several years at the most and maybe a couple of years at the best.

Mr. BARTON. That's good enough for me.

Dr. FAUCI. OK.

Mr. BARTON. Thank you, Mr. Chairman.

Mr. MURPHY. Thank you.

Ms. Castor, you're recognized for 5 minutes.

Ms. CASTOR. Thank you, Mr. Chairman.

GAO's report today identified several areas of concern with our country's ability to surveil, track, and respond to Zika. Dr. Persons, is it accurate that the Zika virus case counts likely underestimated the total number of Zika infections, and would you explain that?

Dr. PERSONS. That's correct. When you talk about the Zika virus, a person can be infected but then not have symptoms in four out of five times. So 80 percent of the folks walking around are called human reservoirs and may not know they have that, and that's where the risk of mosquito control, person-to-person, and/or sexual transmission.

Ms. CASTOR. Right. So given these challenges, how will we be able to conduct predictive modeling to forecast the number of cases in the future and prepare for an outbreak?

Dr. PERSONS. It's going to be a matter of collecting high-quality data, taking models that are currently in existence and trying to

modify them. There are, for example, computational models on sexually transmitted diseases. There's computational models on mosquito-borne and vector-borne diseases, but never the twain shall meet until this point. And so that is going to be a key focus in terms of getting data for that and then testing those models against the datasets as the epidemiology.

Ms. CASTOR. That's not something that we should start and stop. We need a consistent pathway forward.

Dr. PERSONS. Consistent research will be required for something this complex.

Ms. CASTOR. And, Dr. Petersen, I'm aware that there were a number of presumptively positive Zika tests that never went onto confirmatory testing. How many of those are out there?

Dr. PETERSEN. I do not have an exact number, but one of the biggest problems we actually had was in Puerto Rico, because what we found in Puerto Rico is because people who had a previous exposure to dengue—which 90 percent of the population there has—even the confirmatory test could not—for the antibody test—could not separate—even wasn't good enough to differentiate dengue from Zika.

Ms. CASTOR. So was that an issue confined to Puerto Rico, or did we have a presumptively positive Zika test here in the U.S. that also didn't go onto confirmatory testing?

Dr. PETERSEN. The vast majority of women in the Continental United States, we were able to confirm the antibody test result simply because most of those women did not have previous exposure to dengue, which then causes the test to cross-react.

Ms. CASTOR. So how did you decide which specimens would get tested or not?

Dr. PETERSEN. So in the Continental United States, we tested them all with a confirmatory testing as part of the algorithm. In Puerto Rico, we found out that didn't work, and so we stopped that confirmatory test with a test known as the PRNT.

Ms. CASTOR. OK. Since the States and all of the agencies started keeping track of how many—since we started keeping track, how many cases of babies born with birth defects tied to Zika have there been?

Dr. PETERSEN. Right. Well, one of—I do not have that number off the top of my head. I can get back to you with that. What we do know is that this is an ongoing process, because many of the women that have been infected so far have not delivered yet. And so this is an ongoing process of——

Ms. CASTOR. Certainly, the CDC would have, to date, just since we started keeping track, the number of cases of microcephaly and other birth defects tied to Zika, knowing that we have to monitor these babies probably for many years.

Dr. PETERSEN. So I think it's very important to monitor these women as they deliver and see the ultimate impact on their fetuses, both at delivery and long-term consequences. We do know that in the U.S. territories, there's been more than 3,700 women that we've identified who have become infected during their pregnancy and about 1,700 in the Continental United States.

Ms. CASTOR. Right. I have—based upon the CDC update last week, we've had about 5,640 pregnant women with a known Zika

virus. And I was just trying to get to how many we have today born with birth defects, and so if you can please provide that.

And these are heartbreaking consequences for these families. And I do know, based upon recent research, that they are calling this a spike in birth defects across America because of Zika. Would you characterize it that way?

Dr. PETERSEN. I think there is a spike of infections—I mean, of these birth defects simply because this outbreak was so large last year and these women are now delivering.

I was just handed the answer to your question.

Ms. CASTOR. OK.

Dr. PETERSEN. And in Puerto Rico, they're currently reporting 35 cases with birth defects and 72 in the Continental United States. However, we know from our studies that about 10 percent of the women who were infected during pregnancy will go on to deliver a baby that has been affected by Zika virus.

Ms. CASTOR. There are so many other questions, Mr. Chairman. I look forward to the committee's continued attention to this. Thank you.

Mr. MURPHY. Thank you.

I now recognize Mr. Griffith for 5 minutes.

Mr. GRIFFITH. Thank you very much, Mr. Chairman.

And I'm going to start with Dr. Bright. In your just general info on BARDA, it says: BARDA meets its mission by supporting product innovation, advanced development, acquisition and stockpiling, and building manufacturing infrastructure.

Given the threat of emerging, infectious mosquito-borne diseases, would BARDA's mission for developing medical countermeasures also include the development of mosquito-control technology?

Dr. BRIGHT. Thank you for that question. It is a very important question. And currently, the short answer is no, our scope does not include a vector control. However, we have been monitoring it very closely as an innovation in vector control and are considering is there data to support that vector control can also be associated as a medical countermeasure in the reduction of the disease. And so we are working closely with the companies to better understand those technologies.

Mr. GRIFFITH. That's interesting, and I'll see what I can figure out, but I agree. It's probably something that ought to be in your wheelhouse, so to speak.

I'm going to switch and jump off of some of the issues that we've heard today. And Dr. Petersen talked about the situation in Puerto Rico a few minutes ago related to dengue and the testing to determine whether or not Zika is there when you have a population that has been exposed to dengue.

And, Dr. Fauci, that raises the question, when you were testifying about the vaccines and the DNA vaccine where you take a part of the gene of the Zika virus and the body then responds to the protein, because of the close relationship with other diseases like dengue and chikungunya, does that mean that there's a possibility, and should we be looking for it, that the vaccine, for one, will inadvertently or maybe intentionally create a vaccine for all three of those diseases which are so closely related?

Dr. FAUCI. Well, we should be so lucky. But unfortunately, that's not the case. Because even though there's cross-reactivity of antibodies, for example, from Zika to other flaviviruses like dengue and yellow fever, there's not cross-protection. So if you have an antibody against one, you don't protect against, even though they can be confused in a laboratory test. They're not physiologically protective.

But having said that, Mr. Griffith——

Mr. GRIFFITH. I was hoping.

Dr. FAUCI. Well, wait a minute, hope springs eternal. Because having said that, there is work going on right now to actually try and develop a universal flavi vaccine where the component of the vaccine that you present to the body is a common part of the flavivirus that actually is in all the flaviviruses. Whether or not that part is going to induce a protective response is unclear, but there is work thinking exactly as you're thinking right now: Can you actually get a universal—the same ways we're trying for universal influenza vaccine.

Mr. GRIFFITH. All right. I appreciate that. Thank you.

Dr. Petersen, you raised the issue, of course, about Puerto Rico and dengue, and they, of course, had so much exposure last year to Zika that they won't show as much exposure this year because such a large percentage of the population was already exposed. And I was just wondering, what work is being done.

And I'm going to switch gears on you just slightly, so bear with me. I read a report and was somewhat concerned that—even though it was a very small study that—back in March, the American College of Cardiology said that there's a link between Zika and heart disease. And since we have a large population that was, in fact, exposed to Zika, is there any work being done to see if there's a larger study that could be done to determine what the links between Zika and heart disease, if any, are out there?

Dr. PETERSEN. We do not have a specific study looking at heart disease—looking at that link between heart disease and Zika. What we are looking at is of the general spectrum of syndromes associated with infection with the Zika virus, heart disease being just one of them.

There's a variety of neurological conditions that we're looking at as well. So it's part of a longer, larger effort to look at the complete spectrum of disease manifestations with Zika virus.

Mr. GRIFFITH. And when you say you're looking at other neurological issues, that's not just in newborns or the fetus. Is that correct?

Dr. PETERSEN. Correct.

Mr. GRIFFITH. All right. I appreciate that.

Dr. Persons, GAO reports that the grant funds awarded for mosquito control may not make it to some local control districts and that the CDC does not directly monitor mosquito control entities for the use of grant funds.

Assuming that is correct, what do we need to do to make sure that the money we're spending is actually being monitored and it actually goes to where we think it's going, which is to control mosquitos?

Dr. PERSONS. I just thank you for the question, Mr. Griffith. I think persistent oversight, guidance, perhaps changes in policy in terms of the rules or the structure in which CDC does these block grants so that they can be specifically targeted only for mosquito control efforts and not for other things that a State may wish to sponsor, I think is——

Mr. GRIFFITH. I appreciate it.

Dr. Petersen, I'm sorry, I'm out of time. So I would give you a chance, but I don't have the time to respond, so I have to yield back. Or to give you a response.

Mr. MURPHY. Thank you.

Ms. Schakowsky, you're recognized for 5 minutes.

Ms. SCHAKOWSKY. Thank you.

First, let me apologize. I'm the ranking Democrat on a hearing that's going on upstairs, and so I apologize that I missed your testimony.

Given the importance of developing a Zika vaccine, hundreds of millions of Federal dollars have been obligated to conduct clinical trials. I understand there's 32 vaccine candidates that are being studied in the U.S., and the U.S. Government has helped to partially or fully fund a number of those vaccine candidates.

So it's my understanding also that the drug manufacturer Sanofi has received over $40 million from the U.S. Army to conduct a phase 2 trial for one of the vaccines, with the possibility of accessing up to 130 million more in taxpayer funding for phase 3 trials. All told, nearly $300 million of Federal dollars have been obligated for vaccine development to date. So stick with me for a minute.

While it's critical that we develop and manufacture an effective vaccine to combat Zika virus, it's just as critical that the vaccine be available to everyone who needs it. I'm also very concerned that Sanofi recently rejected the Army's request for a, quote, "fair," unquote, price for the vaccine.

Earlier this year, I led 10 of my House colleagues in sending a letter to the Army raising concerns about their plans to issue an exclusive license to Sanofi for the vaccine that U.S. taxpayers helped develop. In addition, Governor Edwards of Louisiana, one of the States that has been hit hardest by the Zika virus, sent a letter to the Army that raised similar concerns.

I'd like to ask unanimous consent to enter both of these letters into the record.

Mr. MURPHY. Could we review this? I'm assuming that would be OK, without objection.

Ms. SCHAKOWSKY. OK. Dr. Fauci, given the enormous investment of taxpayer dollars into the development of a Zika vaccine, do you agree that we need to use every tool of the Federal Government to ensure that the vaccine is affordable?

Dr. FAUCI. The answer to that question is yes, but it is a complicated issue, Congresswoman, as you well know, because we don't really have the mechanisms to influence pricing of a product, even products in which we make a major investment for the development of.

Certainly, we feel, as scientists and public health officials, that the work that we do in the development of vaccines should be available to everyone and anyone who needs it. So, if you're asking

is that the answer to the question, it is absolutely, I feel that we need to do that. Whether or not we have mechanisms in place right now to guarantee that, I don't think we do.

Ms. SCHAKOWSKY. But it is true, isn't it, that vaccines are most effective when the vast majority of the public is immunized? So if it's priced out of reach of many, won't this be a problem in getting control of the whole disease?

Dr. FAUCI. Sure. Yes, it would, obviously, it would be. I mean, if you cannot vaccinate the people who need it—and you correctly said that a vaccine, particularly in an outbreak situation, the more people that get vaccinated, the more control you get over the outbreak. So I agree with you that it's essential, to the extent that we can do that, to vaccinate where appropriate as many people as we possibly can.

Ms. SCHAKOWSKY. It's just a big concern to me since the Army actually said that they would not guarantee a fair price, and yet we're prepared to use taxpayer dollars to lay out perhaps as much as $130 million——

Dr. FAUCI. Right.

Ms. SCHAKOWSKY [continuing]. To them potentially without any ability to control that.

Let me just raise another concern. It's important also to remember the damaging impact that the repeal bill that just passed the House of ObamaCare and the Trump budget would have on Medicaid and our ability to respond to public health crises, like another Zika outbreak.

The per-capita cap included in both the—in TrumpCare and the Trump budget would make it nearly impossible for States to expand services and the number of eligible individuals during a public health emergency, as Michigan did during the Flint water crisis.

Moreover, under a per-capita cap, there is simply no way any State could provide access to a high-priced drug to all of its Medicaid beneficiaries. And depending on how the final Zika vaccine is priced, Medicaid programs could already face challenges in trying to pay for the drug, and those problems would only be compounded if Medicaid was drastically restructured as Republicans have called for.

As this committee investigates the public health response to the Zika virus and considers how we might prepare for future challenges, it's critical to remember the important role that Medicaid has played in responding to public health emergencies and the devastating effect that Republican proposals to cap Medicaid would have on our ability to respond to those emergencies.

I yield back.

Mr. MURPHY. Thank you.

Dr. Burgess, you're recognized for 5 minutes.

Mr. BURGESS. Thank you, Mr. Chairman.

And I would just point out that Bill Clinton, in 1995 and 1996, proposed a per-capita cap for Medicaid because he was worried about running out of other people's money. And he was praised by the editorial board of the New York Times at the time, and every Democratic Senator then sitting wrote a letter to the President wishing him success in that endeavor.

So I actually have a question that I'm going to ask, but it's going to be for the record. We did hear comments about an emergency fund proposed by one of the appropriators. And for just general purposes, we are an authorizing committee. We're not an appropriating committee.

The difference between authorizers and appropriators—and, of course, at the NIH and the CDC you know this—the difference between authorizers and appropriators is there are no buildings named for authorizers. But we are the authorizing committee, and I think we have already authorized that that Representative DeLauro asks for.

And I'm referencing now a compilation of the U.S. Code from January 4, 2012, title 42, chapter 6(a), subchapter 2, Powers and Duties, under part B in general: "The Secretary shall award competitive grants or cooperative agreements to eligible entities to enable such entities to improve surge capacity and enhance community and hospital preparedness for public health emergencies."

So I believe the authorizing language is already there. And so my question that I'm going to submit to you for the record is, is that a correct statement? Do you feel that you have the authorization that you need and now we need to pay attention to the appropriations side of this? Or is, indeed, there different authorizing language that you would require?

Dr. Petersen, let me just ask you, because you—I wasn't going to bring this up, but then you referenced it and so you provoked me, and now I'm going to do it. You said the best way to deal with this disease is to prevent it. And I agree with that. I agree wholeheartedly. And when you said that, I went on your Web site and I looked at your Zika page and I looked at your travel warnings.

And can I just tell you, they're muted. Someone talked about the computational models for the dispersion of this virus throughout various populations. I don't think there was any computational model that predicted what happened in the country of Brazil a few years ago. I mean, I think it caught people by surprise. I don't think the computational models for Ebola 2 years ago quite conformed to what people thought they would.

So while I'm sympathetic to the fact that computational models can help, my concern is, especially with Zika—I mean, I'm one of two States where Zika has been locally transmitted. But, I mean, these are rare, rare, rare conditions. Most of the people that get Zika had to go somewhere and get it and then bring it home to Texas or Florida. Is that not correct, Dr. Petersen?

Dr. PETERSEN. That has been the experience to date as true.

Mr. BURGESS. And, again, along your lines of wanting to prevent it is the best strategy, and I agree with that, I'll just say, I think we should be doing more as far as educating the public. When we've had discussions with the State Department and your agency, it seems to be this: We're pointing to each other to do the work. Someone needs to tell people don't go if you don't want this disease, particularly at certain times of the year.

Now, I recognize that there's certain altitudes you can go to and won't be affected, but generally it is not a good idea, particularly if you're in a family that is contemplating a pregnancy somewhere in the future. Maybe you might not want to do this.

Dr. Borio, let me just ask you—and I know we've talked about this before, but it has been some time ago. And you had in your written testimony the issue of vector control with the Oxitec mosquito.

And there was great concern last summer, this was a public health emergency that was declared by the President, and yet the difficulty with getting the technology for that genetically modified mosquito into areas where it could actually help, it seemed to be very difficult.

In the 1950s, they eradicated the screw-worm fly—and I don't recommend googling that during brunch—but they eradicated the screw-worm fly rather effectively with using that same type of technology, maybe a little bit different now than it was then, but terribly effective.

And one of your statements says that perhaps there's guidance coming from the FDA that we could approach this in a different way now than what we did last August?

Dr. BORIO. Thank you for your question, Dr. Burgess.

So, you know, first, I would just like to stress how important vector control is, and it's an area of unmet need. It's quite challenging to control the vectors that we need to control, as we were till last year, in the areas of local transmission. And as a physician and scientist, I have to stress that this technology seems very promising, and it really deserves to be evaluated more thoroughly. It's in early development, but it deserves its chance to show whether it can assist in this area of unmet need.

The company had a plan to do a field trial in the area of Key Haven, Florida, last year. And for a variety of reasons, including significant resistance by the population that voted against in the local area, the study did not proceed. We continue to maintain a very open line of communication with the company to explore additional studies.

In the meantime, we have published draft guidance that would transfer the authority for oversight of this technology to the EPA, and we are in the comments period right now. We're reviewing comments received.

But the goal for this draft guidance would be to provide a more consistent and cohesive framework for regulating these types of technologies under a more, you know, consistent regulatory agency, which really has a lot of responsibility for vector control when they're for pesticides.

Mr. BURGESS. Thank you.

Mr. MURPHY. Before I recognize Mr. Tonko, Ms. DeGette, you have a request.

Ms. DEGETTE. I just wanted to renew Ms. Schakowsky's request for—unanimous consent request for the two letters, which I agree with them, but also just to make the record complete for Sanofi's response dated May 22, 2017.

Mr. MURPHY. Without objection, those will be accepted.

[The information appears at the conclusion of the hearing.]

Mr. MURPHY. Mr. Tonko, you're recognized for 5 minutes.

Mr. TONKO. Thank you, Mr. Chair.

I'd like to look at the diagnostic testing of Zika. To effectively respond to a Zika epidemic, we must be able to determine who is in-

fected. But diagnostic testing of Zika remains one of the most pressing challenges. There's a number of diagnostic tests authorized by FDA, but these tests have limitations.

GAO's report today identified these challenges. Specifically, GAO stated that certain tests detect the presence of a virus, which may or may not be Zika.

So, Dr. Borio, why has it been difficult for some tests to isolate the Zika virus?

Dr. BORIO. Sure. So these are—there's inherent scientific challenges with developing diagnostic tests for Zika, especially the serological tests. But I think it's important to recognize that all of the tests that have been authorized by the FDA meet performance standards, all of these tests. And if used appropriately, as recommended by the CDC, these tests perform well and should be able to give an answer to patients about whether they've been exposed or infected with Zika virus.

The only remaining challenge today with the tests that are available really has to do with the population in Puerto Rico, which, as Dr. Petersen explained, because of coinfection with other flaviviruses it may not be really possible to make a definitive diagnosis.

Other than that, we have developed—you know, used the limitations of the performance of these tests, but relied on algorithms to be able to give us the answers we need. They all meet standards.

Mr. TONKO. OK. Thank you.

And, Dr. Borio, I also understand that the window during which the Zika virus can be detected is relatively short. How does that complicate diagnostic testing?

Dr. BORIO. Sure. So the window really impacts on the utility of the molecular-based test, the PCR-based test, which is able to detect a virus in the clinical specimen in the acute period of infection. If the window is so limited, it's possible that all the tests might miss detecting the virus when it's present.

For that reason, the CDC algorithm recommends that for those patients for the population that is being tested, a negative test should be followed by the serology test, which measures the antibodies against Zika.

Mr. TONKO. Thank you.

Dr. Persons, according to your report, a total of 15 diagnostic tests are authorized and vary in their performance. But your audit found a number of issues with developing accurate diagnostic tests. So my question is, why is it key that when an infectious disease confronts the U.S. we quickly develop an effective diagnostic test?

Dr. PERSONS. Yes. So thank you, Mr. Tonko, for the question. The answer is simple in terms of the efficacy of the diagnostics goes right to the data that feeds into the epidemiology, which feeds into the clinical treatment, which feeds into the modeling and things that might be required to be more predictive and proactive in these things. So it's all a system that's complex and adaptive, but it hangs together. And diagnostics are very important to this conversation.

Mr. TONKO. So what does it mean for our overall preparedness that there were these difficulties regarding diagnostic test development for the Zika virus?

Dr. PERSONS. I think it just means that in taking a more proactive approach, we need to try and get—a lot of our recommendations are really data or information providing oriented.

For example, if you're a manufacturer, you need to get well-curated data samples to understand, you know, which one contains Zika, in this case, which one does not, so you're really getting down to those very important metrics on performance.

Also, just getting out to the user, so whenever you have the best available science and those numbers, those test results from the diagnostic testing regime, that they get put out to the user base so they efficiently are able to compare apples to apples and do a risk-based analysis at the point of care on which ones might be available and might best be used.

Mr. TONKO. Are there other things that we should be doing differently?

Dr. PERSONS. As I mentioned before, I just think the idea of a more proactive framework on doing that data is gold in this case, so really focusing on that. Putting resources on that data is not going to come for free, but maybe being more expansive about which data you might be able to get.

Again, having a framework for the rapid divulgence of science and best available competitive science as well as information to the marketplace so that they can develop rapidly and go through the regulatory process under EUA in this case.

Mr. TONKO. Thank you very much.

Mr. Chair, I yield back.

Mr. MURPHY. Thank you.

Before we recognize the next, Dr. Burgess, you have a UC request.

Mr. BURGESS. Mr. Chairman, I ask unanimous consent to insert an article from the journal Obstetrics & Gynecology on emerging infectious diseases.

Mr. MURPHY. Without objection, we'll include that article in the record.

[The information appears at the conclusion of the hearing.]

Mr. MURPHY. Mr. Collins, you're recognized for 5 minutes.

Mr. COLLINS. Thank you, Mr. Chairman. I want to thank the witnesses.

If I'm a young woman watching this hearing, I want to ask a few questions because there might still be some confusion. So, Dr. Borio, if a woman wants to know if she has contracted Zika, would you simultaneously recommend she get a PCR test and an ELISA test, I mean, just to pick up either the antibodies or in the PCR?

Dr. BORIO. Dr. Petersen might correct me, but my understanding is that if a woman who is at risk for Zika infection is pregnant, she should be tested. And the algorithm requires that she will have a PCR-based test, and if it's negative, it'll be followed up with a serology test. And that way——

Mr. COLLINS. So you wouldn't do them simultaneously. You'd make her come back a second time?

I mean, if the PCR test is negative—I mean, clearly that—it may have just passed her bloodstream, and then would she have to come back and have another test done? Why wouldn't we do them——

Dr. PETERSEN. Both tests could be done on the same blood sample, so it would not necessarily require her to come back.

Mr. COLLINS. OK. So the protocol would be they draw her blood, they test it with the PCR test. If that comes back positive, well, then she knows she's been infected. If it comes back negative, using the same sample, she doesn't have to come in again. Protocol would be to run through an ELISA.

Dr. PETERSEN. Right. Well, it's complicated, but there's actually two different scenarios. Somebody that has symptoms—as opposed to an asymptomatic pregnant woman. For somebody who has symptoms, the algorithm depends on the time that they present to medical care after their symptoms develop. That will determine what algorithm is actually used.

For an asymptomatic pregnant woman, the current guidelines suggest that she has an IgM test first and an antibody test followed by a PCR test. We are reconsidering those recommendations at the current time, and we expect to have a new algorithm in the upcoming weeks as new information becomes available.

So we are working actually on trying to streamline the testing algorithm to try and make it both simpler for the woman as well as the physician ordering the test.

Mr. COLLINS. I mean, I would think there's a lot of asymptomatic women that just want the peace of mind and that that would be a fairly normal thing.

So another question maybe, Dr. Petersen. We've heard that if a woman is tested positive for Zika, she's not pregnant, do you have a timeframe during which she would feel comfortable or safe in getting pregnant subsequent? Is it 3 months, 6 months, a year? Or at what point in time would a young woman who has tested positive for Zika feel comfortable getting pregnant?

Dr. PETERSEN. Well, there's two issues here. One issue is does infection before conception actually lead to birth defects, and that answer is still not known. We have no evidence that that's the case so far, but out of an abundance of caution, we are advising women to wait—I can't remember the exact number—2 to 3 months—8 weeks. Sorry. Thank you, Tony—8 weeks to conceive after potential exposure.

Mr. COLLINS. Again, that would be good information.

Now, Dr. Fauci, you did mention, you know, the individual thought we might have an HIV vaccine at some point, which we don't. So HIV is an RNA-based virus, so is influenza, so is Zika. So on these viruses that tend to mutate, like that's why we have to come up with a different strain of influenza year after year after year and—what would be different about Zika compared to something like influenza or HIV where we wouldn't have a single definitive vaccine, but yet would have to keep looking at potential mutations each season?

Dr. FAUCI. That's a very good question. And there is a big difference between the mutations of the RNA virus influenza and the mutations of viruses like dengue, like Zika, like yellow fever.

The mutations that are associated with influenza have a major impact on the efficacy of a vaccine. So you can have mutations that have no impact on the virus' phenotype, namely what the virus looks like and how the body sees it. That's not the case with influ-

enza. When influenza makes those mutations, you almost always have to get a new vaccine. That's the reason why we get a new vaccine every season practically.

But when you have other RNA viruses, like flaviviruses, when they mutate, they tend to have mutations that don't have a functional effect, usually. I mean, you'll have an exception to that, but the mutations that generally occur with flaviviruses are mutations that don't impact with the vaccine.

So, for example, yellow fever is an RNA virus. That will have mutations. If you do sequences of one versus the other, you will always see mutations because RNA viruses like to mutate. The critical issue is, is the mutation functionally relevant? And for the most part, for the ones we're talking about today, they're not functionally relevant.

Mr. COLLINS. So that should give us all a little more optimism——

Dr. FAUCI. Yes.

Mr. COLLINS [continuing]. Related to Zika compared to things like influenza.

Dr. FAUCI. You're right. You're absolutely correct.

Mr. COLLINS. Thank you for that clarification.

I yield back.

Mr. MURPHY. Congressman Ruiz is recognized next for 5 minutes.

Mr. RUIZ. Thank you very much.

I'm really glad that we're having this hearing. It's the right topic at the right time. We really sincerely and genuinely have to learn from the past and what we did the first time so that we don't make mistakes that are detrimental to people. And why is that important? Because these are real people who have to take the burden of the human toll.

And what's most distressing to me and we know most distressing to all of us, but me as a physician and now as a father, is the toll it has on children that are born with microcephaly, the developmental problems, the lifelong distress and concern and stress on that kid and the neighborhood and the parents, not to mention, the illnesses that may appear on adults and kids that we still don't know yet but that confirms with Guillain-Barre, heart disease, and other things that may appear 10, 15, 20 years down the road.

So I want to focus on the funding and the approach to pandemics. First, Dr. Petersen, did you get what you asked for? Did the CDC get what they asked for in the initial round? And if not, what was the gap?

Dr. PETERSEN. The CDC got a sufficient amount of funding to then mount a very robust response to the outbreak. It wasn't what we asked for, but it was sufficient to certainly prioritize resources to the highest risk areas, such as Puerto Rico, Texas, Florida, et cetera.

Mr. RUIZ. So when you say that you didn't get what you asked for and yet you say that you have to do the research that you need, if you don't get what you ask for, if you don't get what you need, then that can delay the research that needs to be done in order to expedite a vaccine, expedite treatment, expedite understanding. Correct?

Dr. PETERSEN. I think what's important to know——

Mr. RUIZ. No. I'm asking about whether or not the funds that you get on the front end will affect the time it takes to develop a vaccine and the treatment and the research to understand how to combat it better. Is that correct?

Dr. PETERSEN. Yes.

Mr. RUIZ. Yes. And what are the consequences, therefore, meaning that if you don't have a vaccine, if you don't have a treatment, if you don't understand, then we can be a year, 2 years, 3 years delayed in making sure that we're prepared the next time this happens.

Dr. Fauci, I want to talk about the response and the approach that we did on the last pandemic that approached our territories and also in the U.S. There is a difference between the wait-and-see approach because we just don't have enough information, we don't know what this is going to look like, or the rapid-response prevention so that we can contain a pandemic at the site so it doesn't spread and have a human toll, whether it's in the territories, in the U.S.

Tell me why the wait-and-see approach with pandemics is the wrong approach to treat a pandemic.

Dr. FAUCI. Well, it depends, sir, what you mean by "wait-and-see," to do what? With regard to the vaccine, which I'm responsible for, we didn't wait to see anything. The virus was isolated. It was——

Mr. RUIZ. The wait-and-see approach in terms of, once you identify, do we go and respond to contain the virus or do we wait to see how virulent and how intense or how rapid it will spread?

Dr. FAUCI. Well——

Mr. RUIZ. Do you wait to contain and see what happens, or do you want to go rapid response to prevent it at the scene?

Dr. FAUCI. OK. So that's a question that's a CDC question, and the CDC didn't wait. And I'll hand it over to Dr. Petersen because——

Mr. RUIZ. No. I'm not saying they waited. I'm talking about our ability to fund the programs initially. It was Congress that waited to give the funds.

Dr. FAUCI. Well—OK. So if you're talking about funding, then let's just go back and reframe the answer. When we were aware of the difficulty—both the CDC and ourselves and the FDA and BARDA—we actually proposed a budget for each of us that the President asked for, and we didn't get that until months later. However——

Mr. RUIZ. There was some delay time. And I think that the point I'm making is that there's a latency, and sometimes you don't see the immediate effects of a virus until later through the years, and that all depends on the virus. It's not as gruesome as the Ebola.

Let me take a step back and look at the big picture. If you were a Zika virus and you wanted to wreak havoc on this world and you wanted to infect as many adults and as many children as possible, then you would want to decrease funding to stop or slow down the development of a vaccine, the treatment, or mosquito vector transmission prevention programs, and you would want to decrease funding in the NIH budget and the CDC budget.

If you were a Zika virus and you wanted to infect as many women and children as possible, then you would think about maybe finding a way to deny coverage for maternity care or make it optional——

Mr. MURPHY. The gentleman's time has expired.

Mr. RUIZ [continuing]. And even oral contraceptives. And that's exactly what we have to think about.

Mr. MURPHY. The gentleman's time has expired. I think the gentleman should be careful with the accusations you're saying on that.

Who's next?

Mr. Walberg, you're recognized for 5 minutes.

Mr. RUIZ. For the Zika virus, maybe.

Mr. WALBERG. Thank you, Mr. Chairman.

Dr. Fauci, while much has been learned about Zika virus, we talked about that today, many unknowns remain. With regard to research into the link between the Zika virus and microcephaly, is there any research about other factors? For example, since mercury has been linked to microcephaly for microcephaly cases in northeast Brazil, is any research being conducted on the levels of methylmercury and the mothers of the microcephaly babies?

Dr. FAUCI. To my knowledge, Mr. Walberg, the idea of looking at mercury as a factor in this is not being done, and I believe—not I believe—I know the reason why we're not focusing on that is that the evidence that the virus itself is capable of causing these defects is now pretty overwhelming as being the cause. Now, the idea of there being other secondary cofactors, there's no evidence offhand that there are any other contributing factors such as mercury.

Mr. WALBERG. OK. Well, similarly then, is any research being conducted into the effect that a previous infection with another flavivirus, such as dengue or chikungunya, could have on the rate of severity of microcephaly?

Dr. FAUCI. Yes. That is a good question and a good point. And the answer is, we are looking now from an epidemiological cohort study of individuals who have prior exposure, because there is this phenomenon that may or may not be relevant, we don't know, of antibody enhancement, at least in individuals who get infected with one form of dengue, one serotype and then another serotype. There's no solid evidence that preexisting response to one flavivirus like dengue has an impact on another flavivirus like Zika or yellow fever. There's no evidence yet that that's the case, but we are looking at that.

Mr. WALBERG. OK. Thank you.

Mr. Petersen, what research has the CDC undertaken or what research do you plan to undertake into the link between Zika and microcephaly and other birth defects?

Dr. PETERSEN. Right. So I think we've definitively established that Zika virus causes microcephaly, and I agree with Dr. Fauci, the studies we've done have not identified other cofactors, to date, that would influence that progression towards severe diseases in infants.

It's important that we—to know that we really don't understand the full spectrum of Zika virus infection and its effect on fetuses and children born to mothers exposed to the Zika virus. So it's im-

portant that we continue our birth defects registries, as Dr. Fauci has mentioned, both here and in the U.S. territories so that we can really establish the full spectrum of diseases, disease outcomes associated with this virus.

Mr. WALBERG. Dr. Persons, could you identify some critical challenges that could likely arise with the next emerging infectious disease outbreak?

Dr. PERSONS. So, yes, thank you for the question. The critical challenges we would see, again, is if we're more reactive, you're going to see a lot of the same sort of things. If it's particularly in the case of mosquito-borne, we're going to be much more reactive in terms of how we're dealing with that. We're going to be surging this way and lurching that way as an entire system. You're going to have a lot of rush to try and do something, and then, of course, that's always counterbalanced against the idea of getting, you know, getting data but then getting quality data and then acting upon that data and building your response effectively. So those are the things that we think will continue to happen.

Mr. WALBERG. OK. I yield back.

Mr. MURPHY. Mrs. Walters, you're recognized for 5 minutes.

Mrs. WALTERS. I would like to thank the chairman for holding this hearing and the witnesses for their comments.

On March 31, the California Department of Public Health announced that two breeds of mosquitoes that can carry the Zika virus have been found in 10 California counties, and my district is located in one of those 10 counties.

Dr. Fauci, just recently, it was determined in Laos that there is a third mosquito more prevalently found throughout the United States that can carry the Zika virus. Is this correct?

Dr. FAUCI. Yes, that is correct, Mrs. Walters, but I think it's important to point out, since this subject always comes up, that the demonstration of the potential of a particular mosquito that can transmit the virus is not necessarily correlated with that mosquito in the field transmitting it.

Right now, it's very clear that the overwhelming dominant mosquito that is responsible for this is the Aedes aegypti. Even though there have been studies in the lab where you take a group of mosquitoes of different species and you see if, in fact, the virus can survive in those mosquitoes, and the answer is yes, there are multiple mosquito types that can. The question is, will they, in fact, in the field do that? And there's very strong doubt that that is the case right now.

Mrs. WALTERS. So would you say that this would present any additional risk to the United States?

Dr. FAUCI. No. I wouldn't say zero, but I think that what we've seen over the past now 2 years is the dominance of the Aedes aegypti mosquito. And if you look at, for example, the risk that we've seen now in Florida and in Texas, the mosquitoes that are in that area, the Gulf Coast area, are the Aedes aegypti mosquitoes, and it is almost certain that that's the mosquito that's doing the kind of local transmission that we've seen in Florida and the local transmission that we've seen in Texas.

Mrs. WALTERS. OK. While the Department of Public Health has acknowledged that the transmission risk of Zika throughout the

State of California is low, we must still be diligent in combatting the spread of invasive mosquitoes. Part of that includes education efforts that encourage residents to focus on controlling mosquito growth through proactive measures like eliminating all indoor and outdoor standing water and using window screens. Significant strides have been made, but more work and outreach is needed to avoid a Zika epidemic.

Dr. Bright, what role has mosquito or vector control played in our response to Zika in the United States?

Dr. BRIGHT. Thank you for your question. So right now, the CDC has had the lead on vector control and understanding vector control and repellants and insecticides, and their use and how it will impact and reduce the spread of Zika.

BARDA has not been focused, at this point, as a vector control as a form of a medical countermeasure, so we haven't supported those areas, but CDC has the lead on other vector control.

Mrs. WALTERS. What would you say that the role of the Federal Government should play in mosquito control?

Dr. BRIGHT. I believe if the data would support that vector control and reduction of mosquitoes carrying the disease that can cause significant public health impact, then there would be a significant role for the Government to ensure that that medical countermeasure or that approach is used as an effort to reduce the transmission of that disease.

I do not think at this point we have a significant amount of data that show clearly that even if you reduce the population of certain mosquitoes, it correlates with a reduction of disease in those areas. So we need to get additional data in that area.

Mrs. WALTERS. OK. Is spraying insecticide an effective solution when dealing with breeds that carry Zika?

Dr. BRIGHT. I don't have data on that. I would defer to my CDC colleague, Dr. Petersen, to address that.

Dr. PETERSEN. What we do know is that in Florida, the mosquito-control efforts that we did there appear to have stopped the outbreak in south Florida. It's important to know that spraying pesticides is just one part of a comprehensive strategy to mitigate against vector-borne diseases such as Zika virus.

Mrs. WALTERS. OK.

I yield back the balance of my time. Thank you.

Mrs. BROOKS [presiding]. The Chair now recognizes the gentleman from Pennsylvania for 5 minutes.

Mr. COSTELLO. Thank you. Currently, there is not a specific therapy or vaccine approved for the Zika virus by FDA, but several vaccines are in various stages of development, with one experimental vaccine currently in phase 2 trials being tested in humans.

Dr. Fauci, that's correct?

Dr. FAUCI. Yes.

Mr. COSTELLO. And are there preliminary test results for the vaccine that is in the phase 2 trial?

Dr. FAUCI. Yes. So right now, the data that we have so far in the DNA vaccine, the one to which you're referring, Mr. Costello, is that clearly there are no safety red flags. The signal that we're having is that there does not seem to be any safety issues.

In the phase 1 study, in the early part of the phase 2 study, it has become clear that this vaccine induces the kind of response that you would predict from an extrapolation from the animal model that it would be protective. In other words, the titers of antibody are high enough that are induced by this vaccine that you would make a prediction, if it acts like the virus acts in the nonhuman primate model, that it would be protective upon exposure.

Mr. COSTELLO. And this question may have been asked, I apologize if it has, an updated timeline as to the completion of the vaccine that is in the phase 2.

Dr. FAUCI. Sure. The phase 2a, and now we're going to go into 2b in a few months, is scheduled for about 2,500 individuals. That may go up to 5,000 individuals. The timeline of when you're going to get an efficacy signal is very variable because it depends on two things: one, what the inherent efficacy of the vaccine is, because a very effective vaccine is going to give you a signal more quickly. The other probably more important determining factor is going to be how much infection there is in the community in which you're testing.

So if there's a very, very low level of Zika this coming season, particularly, for example, in the summer in Puerto Rico, it may take a few years before you get enough cases in the vaccine versus placebo to say it works. So that's the reason why, when I answered a similar question, I said it's really unpredictable. It can be as soon as a couple of years, a year and a half, 2, or as far as 3 or 4 or 5 years.

Mr. COSTELLO. Thank you.

Does anyone else have anything to add to that?

If not, I'll yield back.

Mr. BURGESS. Will the gentleman yield?

Mr. COSTELLO. I'd like to yield my time to Dr. Burgess.

Mr. BURGESS. Dr. Fauci, in 2014 when we were dealing with Ebola at the end of August, early September, that we were about at this phase with the Ebola vaccine, then the Ebola epidemic sort of went away, do we have an Ebola vaccine at this point, based on the work that was done in September of 2014?

Dr. FAUCI. Yes. And then I'll get to it just in a sec the difference between those two, and they're really quite different.

So with Ebola, when we did a randomized placebo-controlled trial in Liberia, by the time we got it going and there were enough individuals in Liberia, it just stopped. There were no cases. So you couldn't test the efficacy of it. The similar vaccine—the same one—was used in a ring vaccination trial in Guinea. It wasn't the design of a trial to definitively prove that something worked, but it looked really good from the standpoint of the data.

So we do have vaccine candidates, one of which has some considerable data that it looks like it might be effective, but we haven't definitively proven that yet. And right now, we're doing a trial in Guinea and in Liberia comparing two vaccines: the VSV vaccine, which was the one that was used in the ring vaccination study in Guinea, versus what's called an adenovirus plus an MVA boost from Johnson & Johnson, and we're comparing those two.

Just one last word about the differences between the two is that Ebola is the kind of disease, there's an outbreak, and then it goes away. Just like we've seen right now in West Africa. When you have a mosquito-borne virus like flavivirus, it almost certainly is not going to disappear completely. So we may not have enough cases of Zika in Puerto Rico this summer or in Brazil the next few seasons, but it isn't going to go to zero. And that's the big difference between Ebola and this flavivirus.

Mr. BURGESS. Let me just ask you one other question. Are you to the point with the Ebola vaccine that you can communicate to Dr. Bright that he ought to consider the purchase of that vaccine for the national stockpile?

Dr. FAUCI. I'd yield that to Dr. Bright, but I think his answer is going to be no.

Dr. BRIGHT. Actually, we were quite encouraged by the progress in the development and the data supporting the Ebola vaccines. Again, some of these vaccines could be considered for use in the ongoing outbreak now we're seeing in the Democratic Republic of the Congo.

Mr. BURGESS. But part of the issue is, I guess, what Dr. Fauci said, it was hot as a pistol in August of 2014 and then it's not. So for the utility of BARDA to be able to purchase to provide that substrate that the companies that are manufacturing need the dollars to purchase their product, that's you, right?

Dr. BRIGHT. Yes. So, actually, at least one of these vaccines we do plan to transition over to purchase for the strategic national stockpile for Project BioShield support in this coming fiscal year, in the next fiscal year. It's important to remember that Ebola is not just a public health threat, it is also a national security threat. It is considered and has been deemed a material threat determination. And so we do support the use of those vaccines and procurement of those with Project BioShield.

Mr. BURGESS. Thank you for clarifying.

Ms. Chairwoman, I yield back.

Mrs. BROOKS. Thank you.

The Chair will now recognize myself for 5 minutes.

And staying on that line of questioning, Dr. Bright, as you know, specific language was included in last year's 21st Century Cures to restore the contracting authority back to BARDA as it had been originally executed when the authority was established. And our intent was, in reaffirming the underlying statute, was to remove unnecessary layers of bureaucracy, increase your flexibility, and make sure BARDA can be nimble in making those development decisions without being second-guessed and slowed down through the extraneous layers of review which caused the delays and uncertainty.

And so now that this is law or again it has been made law, what's been the impact of this provision specifically on getting development contracts in place on Zika virus?

Dr. BRIGHT. Thank you for your question. And that's a very important area. And we actually are very grateful that Congress has recognized the need for improved efficiency, especially improved efficiency in our contracting ability and working with industry to be able to move as quickly and nimbly as possible to respond to

emerging threats and in our daily work for other threats that we address for our Nation.

We are grateful for the 21st Century Cures Act and its passage. To date, it has not been implemented yet, as we are waiting for the permanent ASPR to take position hopefully in the near term, and we will be able to work hand-in-hand with that ASPR for full implementation of every provision in the 21st Century Cures Act.

Mrs. BROOKS. So it's actually because the ASPR individual has not been named, confirmed, that is holding up the execution and use for Zika vaccine?

Dr. BRIGHT. We are working very hard at drafting proposals for the ASPR to consider. As you know, BARDA is a part of the ASPR, the Assistant Secretary for Preparedness Response, and so it's critical that we have that permanent ASPR in place to ensure that what we're putting in place for long-term is going to be coordinated and work hand-in-hand with the vision of that ASPR.

We have not yet implemented and changed the contracting authority back to BARDA at this point; however, we are working as efficiently as we can with the ASPR's office of contracting to be able to move forward.

Mrs. BROOKS. OK. And I guess I'd just like to make sure I understand, because that provision was signed into law, and so it's unknown when a permanent ASPR—there's an acting ASPR individual, is there not?

Dr. BRIGHT. There is an acting ASPR, yes.

Mrs. BROOKS. And do we not have the Secretary of Health and Human Services in place that's been in place for some time, does the Secretary realize that that part of the law has not been implemented yet?

Dr. BRIGHT. I'm not able to speak on behalf of the Secretary, but I do know the Secretary recognizes the importance of efficiency and the importance of our ability to work with industry as efficiently and nimbly as possible. I do know that the acting ASPR is working with us on proposals, but we have not moved forward in implementing that yet.

Mrs. BROOKS. Do we have a timeframe on which the acting ASPR is going to, you know, put this matter before the Secretary?

Dr. BRIGHT. I do not have a timeframe on that.

Mrs. BROOKS. OK. How much money was provided to BARDA in 2016 through the emergency funding to assist in the development of a Zika vaccine?

Dr. BRIGHT. In 2016, BARDA received $132 million, and that was distributed for vaccines and diagnostics and our pathogen reduction technologies. So vaccine specifically in 2016, we spent about $94 million.

Mrs. BROOKS. And can you describe then how BARDA did use these funds for the development of the vaccines, the 94 million?

Dr. BRIGHT. Yes. Those funds were to support the technologies we have in our portfolio now, four different companies, who are working on Zika vaccines, and it supported the development and the initial manufacturing of those vaccine candidates and the movement of those vaccine candidates into phase 1 clinical studies. It was with the additional funds we received in fiscal year 2017 from the Zika supplemental, an additional $245 million, they were

able to put to work to move those vaccines and diagnostic candidates into midstage phase 2 clinical trials. And at that point, that is as far as we can move with the funding that we have.

Mrs. BROOKS. Thank you. And I'm going to switch very briefly.

Dr. Borio, one thing we have not brought up and you brought up in your testimony, can you please describe the impact, as quickly as possible, of the Zika outbreak on the blood supply and how those blood supplies are currently being screened?

Dr. BORIO. So this is an area that we have worked very early on to mitigate the threat to the blood supply. Initially, before a screening test became available in the areas of Puerto Rico, for example, BARDA was very proactive and helped us ensure adequate blood supply to Puerto Rico, so the blood supply was imported into the island from the Continental United States. Eventually, blood donor screen tests became available under IND, and those were deployed.

It became apparent last year that, with a number of travelers returning to the U.S., pretty much the entire continent was at risk of the blood supply of the entire United States, and we implemented guidance to make sure that all the blood supply then was screened for Zika.

Mrs. BROOKS. Thank you. Thank you. My time is up.

I now call on Mr. Carter of Georgia for 5 minutes.

Mr. CARTER. Thank you, Madame Chair, and thank all of you for being here. Folks, what we do up here is important, but what you do is lifesaving, and we recognize that. We appreciate all your efforts of that.

I have the honor and privilege of representing the entire coast of Georgia, over 100 miles of coastline where a third of the saltwater marsh in the country on the Atlantic Coast is located. We have mosquitoes. We have them bad. We're concerned about this, and I think rightfully so.

I've had the opportunity to visit a number of mosquito control centers in our area, particularly in the two most populus counties in the coastal region, and they're doing a great job. I dare say that we could not, regardless of Zika, just the mosquito problem, we could not inhabit that area if we didn't have mosquito control, so it's extremely important.

I wanted to ask just a couple of questions real quick. And, first of all, I have a question, Dr. Petersen, about the pregnancy register and registry, because from what I understand, and staff has told me, that there's some concerns that possibly it's not fully effective and that the outcomes that—and we're not getting the outcomes that we should in the people that are listed.

Have you got any concerns with it? Is there anything we can do to assist you to help with any problems you might be having with it?

Dr. PETERSEN. I think that the pregnancy registry so far has been very effective in terms of trying to figure out what the risks of Zika virus infection in the mother is on their developing fetus. What we really don't know and what we need continued support for is trying to figure out the whole spectrum of the illness associated with this virus. And that's just going to take time.

Because what we know now is that some of the babies that may appear completely normal actually aren't. And so trying to figure

out over a period of time and long enough followup is exactly needed to determine what the whole clinical spectrum of this disease actually is.

Mr. CARTER. What's the problem between the territory and Puerto Rico and America? I understand there's a significant difference there in the registry. Is there a reason for that or is there a concern there?

Dr. PETERSEN. Right. So in the beginning, of course, we didn't really know much about the clinical syndrome associated with Zika. In the Continental United States, we took a very—used a very broad definition to try and capture all the potential outcomes associated with this infection. Puerto Rico, on the other hand, used a very narrow definition. They were really focused on the most severe cases of microcephaly. And so that led to some discrepancies in numbers between the Continental United States and Puerto Rico.

However, we have reconciled this. Puerto Rico is now using our case definition for congenital Zika syndrome and will be reporting out shortly similar numbers to what we have in the Continental United States.

Mr. CARTER. OK. All right.

Dr. Borio, I want to ask you about public-private partnerships and how we can use them to speed up the vaccines and the development to market. Have you had experience with these? Is this something that does help that we can work on?

Dr. BORIO. Sure. The FDA has established public-private partnerships. I mean, this is very much a model that we work with to support the vaccine development. We have an important role as regulators, and we have to maintain some firewalls between us and the development.

Mr. CARTER. Right.

Dr. BORIO. But I have to explain to you that, you know, our technical teams are deeply involved with all the different working groups that are developing vaccines and providing very much, in realtime, feedback and active guidance——

Mr. CARTER. Very quickly, any hurdles that you see that perhaps we can assist you with?

Dr. BORIO. No. We deeply appreciate the support we have. We feel like we have the authorities today. And this year, we received resources to be able to support the Zika response. We're in pretty good shape. Thank you.

Mr. CARTER. Good, good.

Very quickly, Dr. Bright, I wanted to ask you, it's my understanding in your testimony you mentioned that you're working with a company in Brazil to come up with a vaccination. Just out of curiosity, their regulations and their licensing arrangements and clinical trial requirements, et cetera, et cetera, are they significantly different from what we have here in America? Can you see of anything that we can do better here in America to help along this line?

Dr. BRIGHT. Thank you. They have an independent regulatory authority, ANVISA. We've worked with the companies in Brazil for the last 10 years in developing, manufacturing, and vaccine development capacity for pandemic influenza and other vaccines, and we've also noticed they are very closely collaborating with our U.S.

FDA. So there's an agreement between our U.S. FDA and the Brazilian regulatory authority that allows them to exchange information and best practices and protocols to accelerate the development of vaccines, actually in our country, as well as theirs.

Mr. CARTER. I'm encouraged to hear that. In fact, I want to compliment all of you. I'm encouraged by what I've heard today, and I appreciate your work on this. And from what I'm hearing, we're making progress. So thank you very much.

And I yield back.

Mrs. BROOKS. Thank you.

The Chair now recognizes the gentleman from Florida, Mr. Bilirakis, for 5 minutes.

Mr. BILIRAKIS. Thank you, Madame Chair. I appreciate it. Thank you for allowing me to sit in on the hearing, because I'm not on this subcommittee, so I really appreciate it. And I want to thank the panel too. I'm from the State of Florida, so obviously we've been affected by the Zika virus, so I appreciate all your assistance. I have a few questions.

Dr. Persons, could you discuss how we can best streamline agency coordination to prevent bureaucratic overlap and redundancies, which can lead to waste and unnecessary delays and hamper the effectiveness of response?

Dr. PERSONS. Thanks, Mr. Bilirakis. So I appreciate the question.

Mr. BILIRAKIS. Sure.

Dr. PERSONS. I'll answer it in two ways. One is GAO has a standard manual for internal controls, and it's called the Green Book. So just the efficacious implementation of those internal control standards, which primarily often have to do with interdepartmental communication and things which often is at the core of this. As you know, all the agencies here have very important—they're doing very important work, very important roles in things, but that systematic look at something and being able to coordinate is easy to say but harder to do and yet very important and critical to a timely response.

The second answer I would say is related to just our overall work. GAO, as you may know, does work on overlap and duplication, and so we have a standing methodology on looking at what constitutes overlap, duplication, or even fragmentation among Federal programs. That report just went out recently, and there's methodology behind the thinking on that that might be commendable to this conversation.

Mr. BILIRAKIS. Thank you.

Next question for Dr. Bright. With a coordinated interagency response, are there interagency goals that drive responsive preparedness strategies? If so, what are those goals?

Dr. BRIGHT. Our goals. So our Assistant Secretary coordinates all of our research efforts and response efforts to the Zika response and other public health emergencies. And so we established, early on in the outbreak, an awareness of the Zika outbreak that we would have interagency alignment and vaccine production and diagnostic production and other countermeasure development. And we established and drafted HHS-wide, U.S. Government-wide goals to achieve the milestones for those vaccines and diagnostics.

Mr. BILIRAKIS. Thank you.

Dr. Petersen, CDC established a Zika registry last year. What data is captured in this registry? How is this data being utilized?

Dr. PETERSEN. So we gather data on evaluations that are done on the mother and fetus throughout pregnancy, and importantly, also on the condition of the fetus and medical consequences of infection following birth. We hope to continue this work and to follow these infants born to mothers infected during pregnancy to determine what the full impact of the virus infection in the mother actually is on the fetus. And that's still an open question.

Mr. BILIRAKIS. OK. What's the value to researchers of tracking beyond 1 year or tracking 5 years? What are the benefits to that?

Dr. PETERSEN. Well, I think the benefits are primarily, number one, telling people what to expect. Two is to provide appropriate medical care and social services for those infants in this condition.

Mr. BILIRAKIS. So you would recommend tracking 5 years as opposed to just one?

Dr. PETERSEN. Recommend follow—excuse me?

Mr. BILIRAKIS. Yes, you would recommend the 5 years?

Dr. PETERSEN. I think we need to follow these infants up for, you know, probably 5 years or possibly even longer, depending on what we find.

Mr. BILIRAKIS. Even longer? Very good. Thank you very much. Good information.

Dr. Persons, earlier this year, the administration released a brief budget outline that proposed a coordination point for Zika-related activity. Can you share observations on how such a central coordinating point could help?

Dr. PERSONS. So, yes, thank you for the question. I think this again is—this incidence with Zika as an emerging infectious disease is one of a kind, and it's unique in one way, but we've seen the pattern before. And so I think as you shift more toward a stronger central coordinating factor, I would say, for example, there's the importance Dr. Fauci mentioned earlier on ASPR and that within or interdepartmental coordination with HHS is certainly critical. There's also sort of a whole-of-Government thing that I think was on display when the previous administration had appointed an Ebola czar back during the Ebola timeframe, just because there are oftentimes things, even outside of big HHS and all the important work they're doing, there's often whole-of-Government response that may involve, for example, DOD, or in this case with mosquito-borne vector disease, you're talking about the regulator of pesticides, EPA, or various other things.

So I think there's some potential commendable thinking on what that central function coordinating might look like even in the whole-of-Government sense on something this complex and this rapidly evolving.

Mr. BILIRAKIS. OK. I want to thank all of you for your efforts, and I look forward to working with you. We can combat this virus. So I really appreciate the testimony.

And I yield back, Madame Chairwoman. Thank you.

Mrs. BROOKS. Thank you to our colleague from Florida.

And to close out——

Ms. CASTOR. Yes. Madame Chair, I wanted to thank you and Congressman Murphy for organizing this hearing on Zika, and thanks to all of our expert panelists.

We've got to remain vigilant and address the funding cliff that's coming up, and also the elephant in the room today with the Trump budget; we're never going to be able to protect our families and businesses across this country if we don't keep America as the world leader in medical research and in disease prevention. Proposed cuts to things like CDC's Center on Birth Defects would come at the exact wrong time when we're seeing an increase in birth defects largely driven by Zika.

Democrats and Republicans came together in the last funding bill and said we are the world leader, and we're going to keep it that way in medical research and disease prevention. And I trust that we can all work together to keep it that way again. And thank you again.

Mrs. BROOKS. And I'd like to thank all of the witnesses. Thank you for your incredible dedication. And I'd like to thank all of your agencies for continuing to work together in the most efficient and most effective way, because the issue of Zika is obviously not going away. Issues of other infectious diseases, whether it's Ebola in West Africa, whether it's cholera in Yemen and other diseases, we must make sure that we as a Government are keeping our citizens safe, that we're learning as much as we can based on all of the outstanding work of your agencies. And we will continue to work with you to make sure that you do have the resources that you need.

And in conclusion, I'd like to thank all the witnesses and Members that participated in today's hearing. Remind Members they have 10 business days to submit questions for the record. I ask that the witnesses all agree to respond promptly to those questions.

And the subcommittee is adjourned. Thank you.

[Whereupon, at 12:37 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON ENERGY AND COMMERCE

May 19, 2017

TO: Members, Subcommittee on Oversight and Investigations

FROM: Committee Majority Staff

RE: Hearing entitled "U.S. Public Health Response to the Zika Virus: Continuing Challenges"

The Subcommittee on Oversight and Investigations will hold a hearing on Tuesday, May 23, 2017, at 10:00 a.m. in 2123 Rayburn House Office Building, entitled "U.S. Public Health Response to the Zika Virus: Continuing Challenges." Last year, the Committee held a hearing on March 2, 2016, entitled "Examining the U.S. Public Health Response to the Zika Virus,"[1] where the Subcommittee examined the emergence of the virus across the Americas, the potential link between Zika and other illnesses, and the public health plan to respond to the virus. The Subcommittee held this hearing early relative to the initial outbreak of the virus and, as a result, the non-partisan Government Accountability Office (GAO) was only able to share preliminary observations in its testimony. On March 23, 2016, the Committee sent a letter to GAO requesting that they finish their work and issue a final report once their work is complete.[2]

At this Subcommittee hearing, the GAO will publicly release its final report entitled, "Emerging Infectious Diseases; Actions Needed to Address the Challenges of Responding to Zika Virus Disease Outbreaks."[3] This hearing will examine the findings and recommendations from the GAO report, as well as lessons learned from the federal government's response to the initial spread of the Zika virus last year. These findings are critical to improving the federal government's response to future outbreaks of the Zika virus and other emerging infectious diseases. The Subcommittee will also hear from federal officials about advancements made in the past year, including in vaccine and diagnostic test development.

[1] *Examining the U.S. Public Health Response to the Zika Virus, Hearing Before the H. Comm. on Energy & Commerce*, 114th Cong. (March 2, 2016), *available at:* https://energycommerce.house.gov/hearings-and-votes/hearings/examining-us-public-health-response-zika-virus.

[2] On file with the Committee.

[3] U.S. Government Accountability Office, *Emerging Infectious Diseases: Actions Needed to Address the Challenges of Responding the Zika Virus Disease Outbreaks*, May 2017, [hereinafter GAO Report]. References to the GAO Report in this memorandum are references to the draft version, on file with the Committee. The final report was not available at the time of drafting. Any changes to final report are not expected to affect information referenced in this memorandum.

I. WITNESSES

- Timothy Persons, Ph.D., Chief Scientist, U.S. Government Accountability Office;
- Lyle R. Petersen, M.D., M.P.H., Director, Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention;
- Luciana Borio, M.D., Acting Chief Scientist, U.S. Food and Drug Administration;
- Anthony Fauci, M.D., Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health; and
- Rick A. Bright, Ph.D., Director, Biomedical Advanced Research and Development Authority; Deputy Assistant Secretary, Office of the Assistant Secretary for Preparedness and Response, U.S. Department of Health and Human Services.

II. BACKGROUND

a. History and Spread of the Virus

Despite medical and scientific advances in the last century, infectious diseases account for one out of every five deaths worldwide.[4] Scientists first identified the Zika virus in 1947 among monkeys living in the Zika forest of Uganda. The first human cases of Zika were detected in Africa in 1952, with the first outbreaks reported on Yap Island in Micronesia in 2007 and French Polynesia in 2013.

The Zika virus spreads primarily through the bite of an infected mosquito. The virus is carried predominantly by the *Aedes aegypti* mosquito, and possibly by the *Aedes albopictus* mosquito, also known as the Asian tiger mosquito.[5] These mosquitoes also carry yellow fever, dengue, and chikungunya. In addition to mosquito bites, the virus can spread through sexual transmission, blood transfusion, and from mother to child during pregnancy.

According to the Centers for Disease Control and Prevention (CDC), the most common symptoms of a Zika infection are fever, rash, headache, joint pain, conjunctivitis (red eyes), and muscle pain. The illness is usually mild with symptoms beginning two to seven days after infection and lasting for several days to a week. In past outbreaks, about four out of five people infected with Zika appeared not to have had any symptoms at all.[6] The high rate of infected

---

[4] GAO Report.

[5] A recent study in a laboratory demonstrated that the *Aedes vexans* mosquito could also spread Zika. *See* https://www.researchgate.net/publication/315061412_American_Aedes_vexans_Mosquitoes_are_Competent_Vectors_of_Zika_Virus.

[6] *Examining the U.S. Public Health Response to the Zika Virus, Hearing Before the H. Comm. on Energy & Commerce*, 114th Cong. (Mar. 2, 2016) (statement of Dr. Thomas R. Frieden, Director, CDC), *available at* https://energycommerce.house.gov/hearings-and-votes/hearings/examining-us-public-health-response-zika-virus.

individuals who are asymptomatic, and therefore do not seek diagnostic testing or medical treatment, makes it difficult to have an accurate case count of Zika virus infections.

Further, a causal link has been established between Zika infection during pregnancy and congenital birth defects. Since the outbreak started last year, there have been numerous reports of microcephaly and other poor health outcomes in babies of mothers infected with Zika while pregnant. Microcephaly is a serious birth defect in which a baby is born with a head smaller than expected and exhibits improper brain development. On February 1, 2016, the World Health Organization (WHO) determined that the rapid spread of Zika infections and the suspected link to microcephaly constituted a "Public Health Emergency of International Concern" under the International Health Regulations.[7] Further, the former Secretary of the U.S. Department of Health and Human Services (HHS), Sylvia Burwell, designated the Zika virus a public health emergency in Puerto Rico in August 2016.[8]

The outbreak in Latin America began in Brazil in February 2015, and was identified as Zika virus in May 2015.[9] As of March 2017, the WHO reported that there are 84 countries, territories, or subnational areas with evidence of vector-borne Zika virus and 13 countries have reported evidence of person-to-person transmission of the virus.[10] Further, there are 31 countries or territories that have reported microcephaly and other central nervous system malformations potentially associated with a Zika infection, or suggestive of congenital infection and there are 23 countries or territories that have reported an increase of incidence of Guillain-Barré syndrome (GBS) and/or laboratory confirmation of a Zika infection among GBS cases.[11]

According to the recent report released by the Government Accountability Office (GAO), 94 percent of all cases in the United States are travel-associated cases, and most of these were associated with travel to the Caribbean, Central America, and South America.[12] Between January 1, 2015, and May 12, 2017, reported Zika virus cases numbered 5,273 in the United States and 36,581 in the United States Territories.[13]

Of the 5,273 cases reported in the continental United States:

- 5,001 cases are travelers returning from affected areas;

---

[7] WHO statement on the first meeting of the International Health Regulations Emergency Committee on Zika virus and observed increase in neurological disorders and neonatal malformations, Feb. 1, 2016, http://www.who.int/mediacentre/news/statements/2016/1st-emergency-committee-zika/en/.
[8] U.S. Department of Health and Human Services, Public Health Emergency, Aug. 12, 2016, *available at* https://www.phe.gov/emergency/news/healthactions/phe/Pages/zika-pr.aspx.
[9] World Health Organization, *Zika: Strategic Response Framework & Joint Operations Plan*, Feb. 2016 [hereinafter WHO Framework].
[10] World Health Organization, *Zika Virus, Microcephaly, and Guillain-Barre Syndrome Situation Report*, Mar. 10, 2017, *available at* http://apps.who.int/iris/bitstream/10665/254714/1/zikasitrep10Mar17-eng.pdf?ua=1.
[11] *Id.*
[12] GAO Report.
[13] Centers for Disease Control and Prevention, Zika Virus, *available at* https://www.cdc.gov/zika/reporting/2017-case-counts.html.

- 224 cases were acquired locally through mosquito-borne transmission in Florida (218) and Texas (6); and
- 48 cases were acquired through other routes, including sexual transmission.

Of the 36,581 cases reported in the United States Territories:

- 143 cases are travelers returning from affected areas; and
- 36,438 cases were acquired locally through mosquito-borne transmission.[14]

The first identified outbreak of mosquito-borne Zika infection in the continental United States occurred in Florida. To date, only two states in the continental United States—Florida and Texas—have documented cases of locally acquired mosquito-borne transmission of the Zika virus. While only two states have confirmed cases of locally acquired mosquito-borne transmission, except for Alaska, every state and three territories have reported cases of Zika.[15]

This month, Brazil announced the end to its Zika public health emergency declaring that from January to April 2017, there were 95 percent fewer Zika cases reported in comparison to the same time period in 2016.[16] This dramatic decline in reported cases is attributable to both Brazil's aggressive mosquito eradication program and herd immunity among the population due to such a large portion of the population being infected by the virus.[17] In the United States, there are no known current active transmission cases.

b. Status of Zika virus research

Research into the Zika virus, particularly into the impact of infection during pregnancy, is ongoing. The National Institutes of Health (NIH) recently implemented a cohort study with a goal of enrolling as many as 10,000 pregnant women at up to 15 sites internationally in order to study the outcome of women who test positive for the Zika virus as well as those who test negative and their infants.[18] The goal of this study is to assess the different risk factors for congenital disease in pregnant women and evaluate the short- and long-term clinical outcomes of babies born to women infected with the Zika virus.[19]

In addition, the CDC established the U.S. Zika Pregnancy Registry, which is used to track and monitor pregnant women who contracted the Zika virus. In the United States, the registry publicly reports biweekly numbers of pregnant women with laboratory evidence of a possible

---

[14] Sexually transmitted cases are not reported for the Territories because, with the local transmission of Zika, it is not possible to determine whether infection occurred due to mosquito-borne or sexual transmission.
[15] GAO Report.
[16] The Atlantic, *Brazil Declares an End to Its Zika Health Emergency,* May 12, 2017, *available at* https://www.theatlantic.com/news/archive/2017/05/brazil-ends-zika-emergency/526509/.
[17] BBC News, *Zika Virus: Brazil Says Emergency is Over,* May 12, 2017, *available at* http://www.bbc.com/news/world-latin-america-39892479.
[18] *Id.*
[19] *Id.*

Zika virus infection.[20] According to the CDC, as of May 15, 2017, there have been 1,409 completed pregnancies with or without birth defects, 58 liveborn infants with birth defects, and eight pregnancy losses with birth defects.[21]

On April 4, 2017, CDC released a report that indicates roughly one in ten women in the United States with a confirmed Zika virus infection during pregnancy resulted in a fetus or infant with virus-related birth defects. The chances of birth defects were even higher among fetuses or infants whose mothers were infected with Zika during the first trimester of their pregnancies.[22]

In addition to the concerns regarding microcephaly, as of March 10, 2017, the WHO has documented 23 countries and territories that have reported an increase in the incidence of GBS or laboratory confirmation of Zika virus infection among GBS cases.[23] GBS "is an uncommon sickness of the nervous system in which a person's own immune system damages the nerve cells, causing muscle weakness, and sometimes, paralysis."[24] "Current research suggests that GBS is strongly associated with Zika; however, only a small proportion of people with recent Zika virus infection get GBS. CDC is continuing to investigate the link between GBS and Zika."[25]

c. Current Status of Diagnostics, Vaccines, and Other Treatments for Zika

Though there are no commercially available diagnostic tests cleared by U.S. Food and Drug Administration (FDA) for the detection of Zika virus, the FDA has authorized two different types of diagnostic tests for the Zika virus—molecular and serologic.[26] Molecular tests are used to detect genetic material of the virus in samples of bodily fluid such as urine or serum. Serologic tests detect antibodies against the virus in blood. The FDA authorized 16 Zika virus diagnostic tests via Emergency Use Authorizations (EUA) during the outbreak—13 molecular tests and three serologic tests.[27] FDA officials later revoked one of the tests, leaving 15 diagnostic tests that are currently authorized.[28]

---

[20] *Id.*

[21] Centers for Disease Control and Prevention, Zika Virus, Outcomes of Pregnancies with Laboratory Evidence of Possible Zika Virus Infection in the United States, as of April 25, 2017, *available at* https://www.cdc.gov/zika/geo/pregnancy-outcomes.html.

[22] Centers for Disease Control and Prevention, Morbidity and Mortality Weekly Report, Vital Signs: Update on Zika Virus-Associated Birth Defects and Evaluation of All U.S. Infants with Congenital Zika Virus Exposure – U.S. Zika Pregnancy Registry, 2016, Apr. 7, 2017, *available at* https://www.cdc.gov/mmwr/volumes/66/wr/mm6613e1.htm?s_cid=mm6613e1_w.

[23] World Health Organization, *Zika Virus, Microcephaly, and Guillain-Barre Syndrome Situation Report,* Mar. 10, 2017, *available at http://apps.who.int/iris/bitstream/10665/254714/1/zikasitrep10Mar17-eng.pdf?ua=1.*

[24] Centers for Disease Control and Prevention, Zika and Guillain-Barre Syndrome, Last Updated Aug. 9, 2016, *available at:* https://www.cdc.gov/zika/healtheffects/gbs-qa.html.

[25] *Id.*

[26] GAO Report.

[27] *Id.*

[28] Zika Virus Response Updates from FDA, *Emergency Use Authorization (EUA),* last updated May 17, 2017, *available at* https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMIssues/ucm485199.htm#eua.

While this number appears high and promising, the GAO found that the tests varied in their performance and operational characteristics—most notable was the variation in the ability of the diagnostic tests to detect the virus and provide accurate results. Each of the existing 15 tests have varying strengths and limitations; therefore, multiple tests and sample types are often required to diagnose an individual with the Zika virus. Furthermore, CDC and FDA guidance are critical in assisting health care providers and laboratories in determining the most appropriate test(s) for each individual.

During the first two weeks after onset of symptoms, Zika can be diagnosed by performing a reverse transcriptase-polymerase chain reaction (RT-PCR) test on serum.[29] This test can accurately determine whether a person has been infected with Zika, but is only effective while the virus is still present in the blood or other fluid. After this initial period, tests to examine the presence of antibodies must be used. These antibodies can persist for several weeks after an infection—currently, an Enzyme-Linked Immunosorbent Assay (ELISA) test is used about four days to 12 weeks post onset of symptoms. However, the presence of similar antibodies from dengue, chikungunya, or even a yellow fever vaccine can cross-react and give a positive result. As a result, a plaque-reduction neutralization testing (PRNT) may be needed to measure virus-specific antibodies and discriminate between cross-reacting antibodies.[30] The PRNT test is described as a highly specialized and lengthy test. GAO found that the delays between getting initial antibody test results and the PRNT confirmatory results may have led some clinicians and patients to make family planning decisions without confirmation of Zika virus infection.[31]

Throughout the developmental stages of the diagnostic tests, manufacturers encountered obstacles including access to clinical samples and other diagnostic tests for comparison purposes. Users of the tests also faced challenges, including determining the most appropriate test to use, access to different tests, and obtaining the equipment needed to conduct the tests.[32] Concerns remain regarding the accuracy of the diagnostic tests and CDC's guidance for testing procedures. A recent report notes that retests of a 2016 batch of samples from Washington, D.C. found that three patients tested positive for the virus, 26 were inconclusive, and 394 remained negative.[33] One of the three positive test results was for a pregnant woman. Since the retesting, CDC has sent updated testing procedures to public health labs throughout the United States.

Currently, there is not a specific therapy or vaccine approved for the Zika virus by the FDA. Several vaccines are in various stages of development, with one experimental vaccine currently in Phase II trials being tested in humans. More vaccine candidates are expected to enter Phase II trials this year. Last month, Dr. Anthony Fauci, the Director of the NIH National Institute of Allergy and Infectious Diseases (NIAID), stated that the DNA vaccine candidate

---

[29] Centers for Disease Control and Prevention, *Diagnostic Testing*, page last updated May 5, 2017, *available at* http://www.cdc.gov/zika/hc-providers/diagnostic.html (last accessed May 15, 2017).
[30] *Id.*
[31] GAO Report.
[32] *Id.*
[33] *3 Retest Positive for Zika in DC; CDC Updates Testing Procedures,* NBC Washington, May 8, 2017, available at: http://www.nbcwashington.com/news/health/3-Retest-Positive-for-Zika-in-DC-CDC-Updates-Testing-Procedures-421656883.html.

developed by scientists at NIAID's Vaccine Research Center had been a success in animal trials and in the first human trial of the vaccine.[34]

d. Vector Control

There are four types of mosquito control methods that are available in the United States: physical control or nonchemical mosquito control, larval mosquito control, adult mosquito control, and using personal protection.[35] According to the CDC, the best way to prevent diseases spread by mosquitoes is to avoid mosquito bites. Official recommendations include using insect repellent, wearing long-sleeved shirts and long pants, protecting your baby or child, and taking steps to control mosquitoes inside and outside your home.[36] For pregnant women, special precautions include not traveling to areas with risk of Zika and using protection during sex during your entire pregnancy due to the risk of infection via sexual transmission.[37]

Additional efforts to prevent the spread of Zika include surveillance of the mosquito population. GAO identified different mosquito control methods that target different stages of the mosquito lifecycle.[38] Therefore, surveillance of the mosquito population is a critical component of preventing the spread of vector-borne diseases such as Zika. The *Aedes aegypti* mosquito can breed in very small containers of fresh water, including in roadside trash, discarded tires, flower pots, and even bottle caps. The mosquito bites during the day and night—and favors biting humans over animals. This characteristic makes the use of pesticides challenging because daytime spraying would be required for the pesticides, or adulticides, to be most effective. Public resistance is a significant limitation to utilizing this method. Further, mosquitoes are becoming increasingly resistant to currently available pesticides. Reduction of the breeding sites is an effective means to control the mosquito population, but this method depends heavily on broad public participation and education. Other emerging technologies continue to be explored, including the release of genetically modified mosquitoes, biological control, and auto-dissemination traps.

In the United States, vector control is handled at the state and local level. The federal government has a very limited role in implementing mosquito control. Many states create mosquito control districts funded by the state, locality, or both. The level of services varies greatly—some local jurisdictions provide services directly, others contract for services with private companies.

While the federal government does not appear to specifically provide funds for mosquito abatement, grants provided by the CDC to states through Epidemiology and Laboratory Capacity (ELC) grants allow for funds to be used to detect, monitor, and control mosquito- and tick-borne

---

[34] CNN, Promising Zika vaccine moves to next stage, April 10, 2017, *available at* http:/www.cnn.com/2017/030/31/health/zika-vaccine-nih-trial/
[35] GAO Report.
[36] Centers for Disease Control and Prevention, *Zika Virus: Prevent Mosquito Bites, available at* https://www.cdc.gov/zika/prevention/prevent-mosquito-bites.html (last updated Jan. 17, 2017).
[37] Centers for Disease Control and Prevention, *Zika Virus: Pregnant Women, available at* https://www.cdc.gov/zika/pregnancy/protect-yourself.html (last updated May 3, 2017).
[38] GAO Report.

diseases in the United States.[39] However, not all localities are served by vector control. Further, grant funds awarded for mosquito control may not make it to some local mosquito control districts. The GAO found that the federal government faced challenges in supporting mosquito control efforts, including sustaining staff expertise in mosquito control during periods when there are no outbreaks, and effectively communicating information about the geographical distribution of mosquitoes that transmit the Zika virus.

e. Unknowns and Challenges Remain

While the scientific and public health communities have learned much about the Zika virus over the past year, the GAO report identifies many areas where unknowns remain, including:[40]

- The total number of infections in the United States;
- The biological mechanisms, risks, reasons for geographic differences, and full spectrum of outcomes associated with mother-to-child transmission;
- The risk of transmission from different bodily fluids and routes, including maternal-fetal transmission;
- The role of prior Zika virus infections or exposure to other related arboviruses; and
- The full spectrum of short-term and long-term outcomes of Zika virus infection, with or without clinical symptoms.

Based on the totality of evidence from epidemiological studies, scientific consensus is now that Zika virus causes microcephaly, brain abnormalities, and other birth defects. The CDC has also reported that its own research suggested a strong association between GBS and Zika virus. At this point in time, we do not know the complete risk of Zika to an individual pregnancy, nor do we know the definitive risk of Zika in causing additional disorders such as GBS. Some researchers have speculated that, in the future, we may see cases where a child presents as normal, but has mental or physical disabilities after becoming infected with Zika in utero.[41] Further, recent research done by the NIH shows that the virus may also have a negative—and possibly long-lasting—impact on male fertility.[42] The research results come from

---

[39] Centers for Disease Control and Prevention, *Epidemiology and Laboratory Capacity for Infectious Diseases, available at* http://www.cdc.gov/ncezid/dpei/epidemiology-laboratory-capacity.html#_blank (last updated Dec. 21, 2016); American Mosquito Control Association, *Funding for National Disease Surveillance Network through Epidemiology and Laboratory Capacity (ELC) Grants from the Centers for Disease Control, available at* http://www.mosquito.org/cdc-funding-position-paper.

[40] GAO Report.

[41] Centers for Disease Control and Prevention, *Morbidity and Mortality Weekly Report, Description of 13 Infants Born During October 2015-January 2016 with Congenital Zika Virus Infection Without Microcephaly at Birth—Brazil,* Dec. 2, 2016, *available at* https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6547e2.pdf.

[42] National Institutes of Health, NIH Director's Blog, *Could Zika Virus Have Lasting Impact on Male Fertility?* Nov. 8, 2016, *available at* https://directorsblog.nih.gov/2016/11/08/could-zika-virus-have-lasting-impact-on-male-fertility/.

a mouse study, which found that the Zika virus can persist for weeks in the reproductive systems of male mice. As a result of the infection, levels of testosterone and other hormones drop, sperm counts fall, and in some cases, the testicles shrink, possibly irreversibly.[43] In addition, we do not know whether individuals who contract Zika but are asymptomatic will have any negative effects for themselves or their children, nor do we know if previous infection from a related virus, such as dengue or yellow fever, has an impact on the effects of Zika on an individual.

Another challenge is the lack of modeling for infectious diseases. Modeling is crucial to combat a virus such as Zika because it would help both public health officials and vector control units prepare for, identify, detect, and predict where the disease is likely to spread. Modeling would also help predict the need for lab and testing capacity in a given region, the demand for vaccines if and when they come to market, and where to prioritize effective mosquito control. The lack of sufficient data, methods, and the unique aspects of the Zika virus pose challenges for conducting modeling and simulation studies. According to CDC documents and officials interviewed by the GAO, the CDC has not been able to predict how much the Zika virus will spread in the continental United States.[44] On May 5, 2017, NIH issued a grant opportunity for "Modeling of Infectious Disease Agent Study Research Projects."[45] According to the announcement, the purpose of this funding opportunity "is to support innovative research that will develop and apply computational tools and methods for modeling interactions between infectious agents and their hosts, disease spread, prediction systems and response strategies."[46]

Finally, challenges remain regarding the development and use of diagnostic tools. Despite the fact that the U.S. has known about the Zika virus, at the time of the discovery that Zika infection during pregnancy could lead to severe birth defects, there were no accurate and reliable authorized diagnostic tools for the Zika virus disease. As previously noted, by April 12, 2017, FDA had authorized 15 diagnostic tests for the Zika virus (12 molecular tests and three serologic tests) under EUAs following the public health emergency declaration. One major issue with these tests is that it is not possible to compare the tests with one another based on the information on the product insert. Communicating such information could have enabled users to more easily identify the test that could detect the smallest amount of virus in a sample.[47]

Manufacturers of diagnostic tests faced several challenges, including: (1) lack of knowledge of key scientific aspects of the virus; (2) difficulty in accessing well-characterized clinical samples; (3) gaining access to EUA tests for use as a comparator assay; (4) gaining cooperation with international entities; and (5) manufacturers' mixed opinions about the effectiveness of communication from FDA.[48] Users of the tests also identified challenges, including: (1) complying with the test's EUA label, which specifies equipment required to perform the test, and (2) determining the most accurate test, in part because of challenges

---

[43] *Id.*
[44] GAO Report.
[45] Grants.gov, Department of Health and Human Services, National Institutes of Health, May 5, 2017, *available at* https://www.grants.gov/web/grants/view-opportunity.html?oppId=293636.
[46] *Id.*
[47] GAO Report.
[48] *Id.*

comparing performance characteristics reported in the EUA labels.[49] GAO found that the CDC and FDA did not follow their guidance in communicating information about Zika virus diagnostic tests that could have enabled users to more easily identify the test that could detect the smallest amount of virus in a sample.[50]

In particular, there were issues with CDC communications about molecular diagnostic test sensitivity. Last year, a CDC scientist and expert on arboroviruses, who later became a whistleblower, alleged that CDC endangered public health when it failed to disclose that the CDC test used to detect the Zika virus, known as a Trioplex (an FDA EUA), was less sensitive than another CDC laboratory-developed test (not authorized under FDA EUA), known as a Singleplex.[51] Following an Office of Special Counsel investigation, CDC agreed to reinstate the scientist. An internal CDC investigation about the allegations found that the evidence did not support the allegations.[52]

The GAO found, however, that the CDC investigation did not attempt to gather additional information on comparing the tests from public health laboratories using the Singleplex.[53] Further, later actions taken by the CDC appear to validate the whistleblower's concerns regarding the Trioplex test. The original Trioplex test was authorized using a smaller input volume, while the Singleplex was not subject to the limitation because it had not been submitted to the FDA for review.[54] Smaller input volume lessens the sensitivity of the test. CDC submitted a substantial amendment to the Trioplex test for FDA authorization to increase the input volume of the test in August 2016, and in January 2017, the authorization was amended again to allow laboratories to use a Singleplex reaction on the Trioplex assay.[55] The larger input volume has been demonstrated to increase the sensitivity of the Trioplex assay, according to CDC. A journal article later showed that the original Trioplex test was less sensitive than the Singleplex test.[56] Representatives of three scientific professional societies told GAO that information about the development and verification of CDC's diagnostic tests should be made available to the scientific and medical communities.[57]

f. GAO Recommendations

The GAO recommended two actions for FDA: (1) Consolidate information from individual diagnostic test labels and make this information available in a form that enables users to more readily compare information across tests; and (2) Require manufacturers to list the

---

[49] *Id.*
[50] *Id.*
[51] Lena H. Sun, CDC whistleblower claims agency has been using wrong Zika test, Washington Post, September 28, 2016.
[52] U.S. Department of Health and Human Services, Report of Investigation, OSC File Number DI-16-3709, attached to September 2, 2016 from HHS Secretary Sylvia M. Burwell to The Honorable Carolyn N. Lerner, Special Counsel, Office of the Special Counsel.
[53] GAO Report.
[54] *Id.*
[55] *Id.*
[56] *Id.*
[57] *Id.*

identity of comparator assays on their diagnostic test labels. The FDA concurred with both recommendations.

The GAO recommended three actions for CDC: (1) Establish a transparent process to provide CDC diagnostic tests, upon request, to manufacturers that are in the final stages of diagnostic test authorization; (2) Include information on CDC-developed tests distributed to public health laboratories on CDC's website, including any laboratory-developed tests; and (3) Provide details such as collection records, dates, and data limitations on posted and disseminated mosquito distribution maps to better inform mosquito control experts and the general public. CDC concurred with Recommendations (1) and (3), and partially concurred with Recommendation (2).

In recent decades, emerging infectious diseases have continued to garner global attention. Diseases such as SARS, H1N1, Ebola, pandemic influenza, and now Zika have continued to surface leaving little time for public health officials to react. In each of the aforementioned cases, the GAO found that HHS was reactive in its response to outbreak prevention, preparedness, detection, and response. This was the theme of the Subcommittee's hearing on biodefense preparedness held on February 12, 2016, focused on the bipartisan report of the Blue Ribbon Study Panel on Biodefense.[58] Given global travel and migration patterns, infectious diseases spread more easily than ever before. With the emergence of more infectious diseases around the corner, the federal government needs to find ways to be more proactive instead of reactive.

g. Status of Zika Funding

Funding for federal government spending on the Zika virus has come from multiple sources. On April 6, 2016, the White House Office of Management and Budget and the Secretary of HHS identified $589 million that could be redirected and spent on the response to the Zika virus.[59]

In addition, through the Zika Response and Preparedness Act, 2017, Congress provided an additional $1.1 billion in supplemental funds to the U.S. Department of Health and Human Services, the U.S. Department of State, and the U.S. Agency for International Development. HHS received $933 million of the $1.1 billion. Of the $933 million, the CDC received $394 million, the NIH received $152 million, and the Public Health and Social Services Emergency Fund received $387 million, with $245 million of that going to the Biomedical Advanced Research and Development Authority (BARDA).[60]

As of April 30, 2017, HHS has obligated $635 million of the $933 million appropriated in the Zika Response and Preparedness Act.[61] The breakdown by agency is as follows:

---

[58] *Outbreaks, Attacks, and Accidents: Combating Biological Threats, Hearing Before the H. Comm. on Energy & Commerce*, 114th Cong. (Feb. 12, 2016), *available at* https://energycommerce.house.gov/hearings-and-votes/hearings/outbreaks-attacks-and-accidents-combatting-biological-threats.
[59] Congressional Research Service, *Zika Response Funding: Request and Congressional Action*, Sept. 30, 2016.
[60] U.S. Dep't of Health & Human Servs., *Zika Supplemental Funding Spend Plan*, Oct. 26, 2016.
[61] Email from HHS staff to Committee staff, May 18, 2017.

- CDC: $332.2 million obligated;
- NIH: $68.8 million obligated;
- ASPR/BARDA: $110.6 million obligated;
- HRSA: $57.3 million obligated; and
- CMS: $66.1 million obligated.

HHS has informed the Committee that remaining funds not yet obligated have been committed, and that the funding will last through the end of the fiscal year.

III. ISSUES

The following issues will be examined at the hearing:

- How can the CDC and the states be better equipped to respond to any potential Zika outbreaks in the U.S. this summer?
- How can the FDA and CDC establish a transparent process for providing test manufacturers access to diagnostic tests for comparison purposes and provide information to help ensure that users of diagnostic tests can compare performance?
- How can state and local implementation of mosquito control programs be improved and more effectively supported by federal agencies?
- What is the current state of research into (a) the causal link between Zika and other health conditions, including microcephaly and GBS; and (b) the efficacy and availability of currently available rapid diagnostic testing for Zika?
- What is the status of diagnostic testing development, vaccine development, or other therapeutics for Zika?

IV. STAFF CONTACTS

If you have any questions regarding the hearing, please contact Alan Slobodin, Brittany Havens, or Jennifer Barblan at (202) 225-2927.

Congress of the United States

Washington, D.C. 20515

February 15, 2017

Robert M. Speer
Acting Secretary of the Army
101 Army Pentagon
Washington, DC 20310-0101

Dear Acting Secretary Speer:

We write to you to strongly urge the Department of the Army not provide an exclusive license to Sanofi Pasteur, Inc. for two pending patents to manufacture the Zika vaccine. If such a license is issued, we are very concerned that the price of the vaccine, which was developed with taxpayer dollars, will be unaffordable for people in the United States and around the world. As you know, the cost of the drugs is one of the most pressing public health concerns and rising drug costs continue to harm patients who need access to those drugs and taxpayers who both pay to develop many drugs and fund public insurance programs like Medicare and Medicaid.

Our concerns have been echoed by organizations such as Doctors Without Borders, who fear that without safeguards in place to ensure the vaccine is affordable, it will be inaccessible to people in developing countries who can ill-afford such costs. Moreover, President Trump has repeatedly called for action to lower drug prices, and we fear awarding an exclusive license for a critical vaccine developed with public funds to a single drug manufacturer will set a dangerous precedent.

When the Zika virus surfaced and infectious disease experts at the National Institutes of Health (NIH) determined the threat it posed to the American public, it became a national priority for Congress to take swift action and allocate funding for developing an effective vaccine to combat the spread and infection of the Zika virus. As a result, Congress acted to provide NIH with more than $40 million to develop and test such a vaccine. Despite that substantial investment by taxpayers, on December 9th, the Department of the Army filed with the Federal Register a Notice of Intent to grant Sanofi exclusive licenses for two pending government patents to manufacture the Zika vaccine. The Notice of Intent would give Sanofi a monopoly for the Zika vaccine without any restrictions or requirements that they ensure the vaccine is affordable for all those who need it.

In order to ensure that the investment made by taxpayers was worthwhile, it is critical that we ensure the vaccine to prevent against the Zika virus is accessible to anyone who requires it. Again, we strongly urge the Department of the Army not provide an exclusive license to Sanofi

to manufacture this vaccine. If the Department of the Army does decide to move forward with their proposal, we implore you to instead issue a limited license and put in place requirements that this vaccine must be available at an affordable price and allow the federal government to intervene if Sanofi prices the drug at a level that would make it inaccessible to the millions of Americans who need access to a vaccine they paid to develop. Without these changes, we are fearful that Americans and people in developing countries will not be properly protected against future outbreaks of the Zika virus.

We look forward to your response, and to working with the Administration to ensure that the price of the Zika vaccine does not threaten public health by deterring access to this vital therapy.

Sincerely,

JAN SCHAKOWSKY
Member of Congress

LLOYD DOGGETT
Member of Congress

JOHN CONYERS, JR.
Member of Congress

JUDY CHU
Member of Congress

MARK POCAN
Member of Congress

ROSA L. DELAURO
Member of Congress

PRAMILA JAYAPAL
Member of Congress

KEITH ELLISON
Member of Congress

MICHELLE LUJAN GRISHAM
Member of Congress

ELIJAH E. CUMMINGS
Member of Congress

PETER WELCH
Member of Congress

Cc: Francis Collins, Director, National Institutes of Health

Anthony Fauci, Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health

Office of the Governor
State of Louisiana

JOHN BEL EDWARDS
GOVERNOR

P.O. Box 94004
BATON ROUGE, LOUISIANA 70804-9004
(225) 342-7015
GOV.LA.GOV

May 10, 2017

Robert M. Speer
Acting Secretary of the Army
101 Army Pentagon
Washington, DC 20310-0101

Dear Mr. Speer,

As Governor of the State of Louisiana, I write to express my serious concern about the Department of Defense's proposed exclusive license of patents on a Zika vaccine to Sanofi, particularly if the license does not address the pricing of the vaccine to U.S. residents.

Louisiana remains one of the Gulf states most likely to be affected in the event that the Zika virus continues to spread. A decision to give one company, Sanofi, a monopoly, without any constraints on the price for the vaccine, could cripple state budgets and threaten public health in the event of local Zika transmission. As many as 540,000 Louisiana residents on Medicaid alone could benefit from an effective Zika vaccine, but all my constituents deserve access in the event of local transmission. I am concerned that an unaffordable Zika vaccine will unnecessarily expose our state's most vulnerable citizens, our babies, to risk for serious lifelong complications of preventable Zika infection.

It is my understanding that considerable federal support has gone into creating the vaccine, including federally-funded clinical trials, a $43 million BARDA grant to Sanofi for Phase II trials, with the option for an additional $130 million in funding for the later trials if needed for the vaccine's approval by the FDA. Sanofi would also be eligible for a valuable priority review voucher, worth millions of dollars, and possibly benefit from several years of exclusive rights on the data from the clinical trials the U.S. government has funded. The extent of public investment in the development of the vaccine calls into question the need for an exclusive license, and it certainly provides a compelling reason to ask questions about the price of the vaccine now, before a license is signed, rather than after a monopoly has been granted.

Furthermore, because the vaccine in question is the Zika Purified Inactivated Virus (ZPIV) and makes use of the inactivated virus to produce an immune response, it may have added benefits and value as a booster vaccination to DNA Zika vaccines. Preliminary studies by NIAID found that the ZPIV induced antibodies that neutralized the virus and protected animals from disease when they were challenged with Zika.

I am concerned that the Department of Defense has yet to address concerns about pricing and affordability for the vaccine, despite requests from nearly a dozen non-governmental organizations representing patient interests. In April 2017 the Department of Justice ordered Sanofi to repay nearly $20 million in overcharges to the Department of Veterans Affairs. Sanofi is known to charge U.S. residents far more than residents of other industrialized countries for other medications, such as Sanofi's multiple sclerosis drug Aubagio (teriflunomide).

We believe our interests would be better served by avoiding the grant of an exclusive license on the Army's Zika patents. Barring that, U.S. residents, particularly those that I represent in Louisiana, deserve assurances that the vaccine will be affordable to people who have already paid for most of the research and development costs.

No one should have to worry about their child being born with microcephaly or other birth defects, and certainly no one should have to face that frightening prospect simply because the vaccine is unaffordable. Louisiana taxpayers have already paid once for this invention, and it is reasonable to expect that the Department of Defense at minimum ensure that our residents pay reasonable prices on the other end.

Sincerely,

John Bel Edwards
Governor

cc: Barry Datlof

May 22, 2017

The Honorable Tim Murphy
Chairman, House Energy and Commerce
Oversight & Investigations Subcommittee
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Diana DeGette
Ranking Member, House Energy and Commerce
Oversight & Investigations Subcommittee
2125 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Murphy and Ranking Member DeGette:

Thank you for scheduling a hearing on the U.S. Public Health Response to the Zika Virus: Continuing Challenges. Sanofi Pasteur, the vaccines division of Sanofi, is pleased to participate in this effort by partnering with the Walter Reed Army Institute of Research (WRAIR) and the Biomedical Advanced Research and Development Authority (BARDA) on a Zika vaccine candidate, an important component of Zika response.

The development of any vaccine is a high-risk endeavor, particularly for emerging infectious diseases marked by changes in epidemiology and trajectories that are still evolving. In fact, in November of 2016, the World Health Organization indicated the Zika outbreak is no longer a public health emergency. That was followed by the government of Brazil on May 12, 2017, declaring an end to its Zika public health emergency after 95% fewer cases were recorded between January and mid-April, 2017, compared to the same period the prior year. Each of these examples underscores the unpredictability of seasonal endemic diseases. To effectively address these types of public health challenges, it is essential for vaccine manufacturers to collaborate with governmental scientific organizations to effectively leverage our complementary resources, expertise, and strengths.

In advancing this Zika vaccine candidate in collaboration with the U.S. government, we have contributed significant resources, including over 60 full time scientists, proprietary technical manufacturing expertise, and utilization of our robust flavivirus clinical trials network to bring the vaccine candidate through Phase II studies. Sanofi Pasteur has engaged in this endeavor in the face of opportunity costs associated with delaying other R&D programs in order to advance this vaccine at an unprecedented pace. Despite claims to the contrary, we do so not based on projected commercial return, but out of our sense of corporate responsibility to contribute our capabilities to address a potential public health crisis.

Significant attention has been paid to whether our public-private partnership with the WRAIR may constitute a monopoly for Sanofi Pasteur. Questions have also been raised regarding the potential pricing of a future Zika vaccine. In truth, dozens of other companies, many with funding from the U.S. government, are also developing Zika vaccine candidates, some using similar approaches, others using other novel technologies. It is unclear at this time which approach, if any, will ultimately succeed. However, as we continue to negotiate the terms of a licensing agreement with WRAIR for its patents, and whether that agreement ultimately is exclusive or non-exclusive, our potential license would not cover all vaccine technologies and thus would not prevent other companies from pursuing vaccine candidates based on alternative technologies in order to create a robust and competitive Zika vaccine marketplace.

SANOFI

Additionally, it is premature to consider or predict Zika vaccine pricing at this early stage of development. As noted earlier, ongoing uncertainty around epidemiology and disease trajectory make any commercial projections theoretical at best. However, if we ultimately reach a licensing agreement with the WRAIR and bring a Zika vaccine to market, Sanofi Pasteur has a history of working with governments and non-governmental organizations around the world to make our vaccines available at affordable prices. Evidence of our commitment to safe, affordable, and accessible vaccines is demonstrated by our industry-leading ranking on the Access to Vaccines Index (https://accesstovaccinesindex.org/report-cards/sanofi/) and the publically available pricing of our products both in the United States and abroad. It is in the public-health interest to price this and other vaccines in a way that will facilitate access to and usage of a preventive vaccine. We have demonstrated that commitment in the past, and, if we bring a Zika vaccine to market, we intend to do so for Zika as well.

Given the many uncertainties surrounding the future of Zika, we believe the WRAIR and BARDA are to be commended for their approach to partnership with industry. In fact, given the high risk nature of vaccine development and unpredictability for diseases like Zika, if the U.S. government changes its historic approach to licensing terms, it could undermine the intent of these types of collaborations.

Sincerely,

[redacted]

Adam Gluck
Vice President and Head, U.S. Government Relations
Sanofi

Cc:

The Honorable Morgan Griffith
The Honorable Joe Barton
The Honorable Michael Burgess
The Honorable Susan Brooks
The Honorable Chris Collins
The Honorable Tim Walberg
The Honorable Mimi Waters
The Honorable Ryan Costello
The Honorable Buddy Carter
The Honorable Greg Walden
The Honorable Janice Schakowsky
The Honorable Kathy Castor
The Honorable Paul Tonko
The Honorable Yvette Clarke
The Honorable Raul Ruiz
The Honorable Scott Peters
The Honorable Frank Pallone

Clinical Expert Series CME

Emerging Infectious Diseases in Pregnancy

Richard H. Beigi, MD, MSc

It has been recognized for centuries that pregnant women have unique susceptibilities to many infectious diseases that predispose them to untoward outcomes compared with the general adult population. It is thought a combination of adaptive alterations in immunity to allow for the fetal allograft combined with changes in anatomy and physiology accompanying pregnancy underlie these susceptibilities. Emerging infectious diseases are defined as those whose incidence in humans has increased in the past two decades or threaten to increase in the near future. The past decade alone has witnessed many such outbreaks, each with its own unique implications for pregnant women and their unborn fetuses as well as lessons for the health care community regarding response and mitigation. Examples of such outbreaks include, but are not limited to, severe acute respiratory syndrome, the 2009 H1N1 pandemic influenza, Ebola virus, and, most recently, the Zika virus. Although each emerging pathogen has unique features requiring specific considerations, there are many underlying principles that are shared in the recognition, communication, and mitigation of such infectious outbreaks. Some of these key principles include disease-specific delineation of transmission dynamics, understanding of pathogen-specific effects on both mothers and fetuses, and advance planning and contemporaneous management that prioritize communication among public health experts, clinicians, and patients. The productive and effective working collaboration among the Centers for Disease Control and Prevention, the American College of Obstetricians and Gynecologists, and the Society for Maternal-Fetal Medicine has been a key partnership in the successful communication and management of such outbreaks for women's health care providers and patients alike. Going forward, the knowledge gained over the past decade will undoubtedly continue to inform future responses and will serve to optimize the education and care given to pregnant women in the face of current and future emerging infectious disease outbreaks.

(Obstet Gynecol 2017;129:896–906)
DOI: 10.1097/AOG.0000000000001978

Emerging infectious diseases are defined as pathogenic outbreaks whose incidence in humans has increased in the past two decades or threaten to increase in the near future.[1] The importance of emerging infectious diseases has been recognized for at least 20 years and continues to increase in importance and scope for many societal and ecologic reasons.[2,3] Such outbreaks of novel pathogens frequently cross national and territorial boundaries (in part as a result of the robust travel of modern life) and include recently highlighted and severe pathogens such as severe acute respiratory syndrome (SARS), the 2009 H1N1 pandemic influenza, Ebola virus, and, most recently, the Zika virus. In addition to these highly publicized outbreaks of recent times, emerging pathogen terminology also includes less dramatic, but often no less menacing, considerations such as 1) new infections resulting from changes or evolution of existing organisms, 2) known infections spreading to new geographic areas or populations, 3) previously unrecognized infections appearing in areas undergoing ecologic transformation, and 4) old infections reemerging as a result of the development of antimicrobial resistance to known standard agents or

From the Department of Obstetrics, Gynecology, & Reproductive Sciences, Magee-Womens Hospital of the University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania.

Continuing medical education for this article is available at http://links.lww.com/AOG/A942.

The author has indicated that he has met the journal's requirements for authorship.

Corresponding author: Richard H. Beigi, MD, MSc, Department of Obstetrics, Gynecology, & Reproductive Sciences, Magee-Womens Hospital of UPMC, 300 Halket Street, Pittsburgh, PA 15213; email: rbeigi@mail.magee.edu.

Financial Disclosure
The author did not report any potential conflicts of interest.

ISSN: 0029-7844/17

breakdowns in public health measures.[1–3] Commonly cited emerging infectious diseases of interest and some pathogen specifics are compiled in Box 1.

It has been appreciated for centuries that pregnant women have unique immunologic and physiologic characteristics that predispose them to heightened rates of serious and sometimes fatal outcomes from varied infectious diseases. This observation is mostly attributed to the combination of somewhat altered cellular immunity capabilities (presumably to allow for the fetal allograft) combined with changing anatomic specifics that can challenge primarily cardiovascular and respiratory systems with advancing gestational age.[4–9] More recent research has focused on relative concentrations and potencies of various immunoglobulins (immunoglobulin G) during pregnancy as part of the explanation for altered pregnancy immunity.[10] Additionally, ongoing investigations are assessing the role of the placenta and its inherent ability to block some viral pathogens from access to the fetus.[11] Ongoing research will continue to delineate the specifics of the immunology of pregnancy and its effect on disease transmission and pathogenesis.

The heightened susceptibility to adverse outcomes is most often noted for viral pathogens, with bacterial and parasitic infections occasionally also having this predilection. In addition, pregnant women also have unique characteristics worthy of attention with regard to infectious diseases (and their countermeasures) from clinicians including, but not limited to, the teratogenic potential of an infecting pathogen, differing transmission susceptibilities and specific implications for fetal infection during different stages of pregnancy, and the effect of an in utero infection on subsequent neonatal and infant development. Importantly, despite a predilection for worse outcomes, it does not appear (for the majority of pathogens) that pregnancy makes women more susceptible to acquiring an infection with the possible exceptions of human immunodeficiency virus, malaria, and potentially listeriosis.[12]

In addition to the inherent risks posed by emerging infectious diseases to pregnant women, the concept of the medical establishment's preparedness and response in the face of novel outbreaks has also recently received considerable attention. Much of the early focus toward preparedness was centered on the likelihood of an impending influenza pandemic.[13,14] However, the concepts and collaborations have now matured to include guidance and directives that are simultaneously relevant for a broad range of pathogens as well as specific outbreaks.[15–17] This is most recently evidenced by the appropriate attention received by, and prioritization given to, the ongoing Zika virus outbreak. A robust collaboration among the Centers for Disease Control and Prevention (CDC), the American College of Obstetricians and Gynecologists (the College), and the Society for Maternal-Fetal Medicine has also been paramount in highlighting important up-to-date knowledge, thereby enabling practice that is based on the best available data during the evolution of Zika and others. The

Box 1. Commonly Noted Emerging and Reemerging Pathogens of Interest

Pandemic influenza viruses

Novel influenza strains, emerging from antigenic shift in the influenza virus, causing occasional severe influenza pandemics

SARS-associated coronavirus

Highly pathogenic, novel severe respiratory virus that emerged and rapidly spread globally from a small location in China

Ebola virus

Previously recognized serious pathogen associated with modest-sized outbreaks before 2014 (largest outbreak); strikingly high mortality rate

Zika virus

Previously underappreciated pathogen until ongoing outbreak with its association with fetal malformations (most notably microcephaly); its unique characteristics put this outbreak at the intersection of emerging infectious diseases, reproductive rights, and global health security

West Nile virus

The most common mosquito-borne infection in the United States; no documented direct fetal effect

Chikungunya virus

Mosquito-borne virus that was previously found in Asia, Africa, and Europe that has recently been detected in the Americas; no documented direct fetal effect

Methicillin-resistant *Staphylococcus aureus*

Well-known reemerging pathogen given its aggressive clinical nature and relatively limited antimicrobial treatment options

Vancomycin-resistant enterococci

Classic reemerging pathogen that serves as an ongoing reminder of the ever present and evolving epidemic of antimicrobial resistance

SARS, severe acute respiratory syndrome.

women's health field has successfully aligned in response to these recent outbreaks in a manner that will undoubtedly serve pregnant women optimally. This article highlights a series of recent high-profile, specific emerging pathogens of significant maternal–fetal importance given their important lessons to the obstetric and public health community. In addition, the pathogens chosen for discussion have some unique and challenging features and provided unique foundations for progress in the area of health care provider, facility, national, and international preparedness planning and disease mitigation.

SEVERE ACUTE RESPIRATORY SYNDROME

Severe acute respiratory syndrome is a previously unrecognized emerging infectious disease caused by a novel pathogen that challenged the global health community's ability to effectively communicate and cooperate toward a goal of eventual containment. Believed to have originated in China's Guangdong Province late in 2002, it appears to have been spread internationally in the winter of 2003 by a physician who had traveled to the region to provide care against a new mysterious respiratory pathogen. Traveling home from China, he stayed one night at what later came to be referred to as Hotel M (from the epidemiologic perspective) in Hong Kong and was noted to have been ill for approximately 7 days prior with the same respiratory symptoms as his patients. Subsequent to his short, 24-hour stay, approximately 12 additional guests fell ill from this same unknown pathogen (the majority of whom were staying on the same floor as him in the hotel, yet without significant close contact) and then proceeded to travel abroad and perpetuate the global spread of what is now known as SARS. Involved countries included Canada, Vietnam, Singapore, Ireland, and the United States. In total, the World Health Organization (WHO) recognized at least 8,400 associated cases, with more than 800 deaths in greater than 32 countries recorded over roughly 6 months.[5,18] It was accordingly dubbed the first 21st century pandemic.

The infection was characterized by a rapid onset of fever plus other nonspecific symptoms (headache, malaise, and myalgia) followed by a nonproductive cough that progressed to shortness of breath and respiratory failure in a subset of patients. Characteristic laboratory aberrations include lymphopenia and elevated lactate dehydrogenase levels. The causative agent was later noted to be a novel coronavirus likely present in animals being sold in local markets and subsequently infecting those handling the animals (zoonotic spread). Importantly, the subsequent human-to-human spread was through respiratory droplets, yet early on, given the many unknowns, infection control practices included all phases of precautions: respiratory, contact, and droplet.

Cohorting (grouping of persons [patients or health care workers] who have been exposed to a disease, a form of isolating groups to minimize disease spread within in a location) and isolating of patients in facilities as well as widespread public education, contact tracing, quarantine practices, border surveillance, and travel advisories were instituted and successfully contributed to the eventual global control within approximately 5 months of first notification.[5,18] In the few affected obstetric hospitals, close attention was paid to minimizing exposure to unaffected patients and staff by way of cohorting exposed and infected patients, visitor limitations, vigilance toward the use of personal protective equipment (such as masks and gowns), clinical flexibility, facility temporary closure, working collectively to establish coordinated and regionalized care, and a willingness to consider and establish care models that minimized mixing of patients and obstetric health care providers.[18,19] All of these nonpharmaceutical interventions are important for all facilities providing care to pregnant women to consider and plan for in advance. This is a key lesson from the SARS epidemic; traditional nonpharmaceutical countermeasures are very effective for curbing disease spread, even in the absence of pharmaceutical interventions.

Understanding the effects of SARS on pregnancy is more challenging given the relatively low numbers of women infected. The few small available case series suggest that pregnant women had at least equal, and likely higher, rates of severe illness, intensive care unit admission, and death (similar to other serious respiratory pathogens in pregnancy).[18,20] As noted in other severe respiratory infections, some women underwent preterm cesarean delivery presumably for maternal respiratory benefit. No documented cases of perinatal transmission were noted despite relatively rigorous methods of investigation for viral particles, serologic responses, or both in neonates born to infected mothers. The low numbers of infected pregnant women were also attributable in part to the critically important and rigorous infection control practices noted (cohorting, regionalization of care, minimizing patient and health care worker mixing, use of personal protective equipment) used in hospitals that were successful in interrupting disease transmission.[18–20] The importance of the traditional infection control measures in and of themselves cannot be overemphasized. Important lessons for obstetric health care providers,

Box 2. Important Lessons Learned for Health Care Providers and Facilities From Select Recent Emerging Infectious Disease Outbreaks

SARS virus

- Novel emerging pathogens originating abroad can become local problems quickly given international travel patterns and methods of transmission
- Globally coordinated nonpharmaceutical responses to infectious disease outbreaks are critically important for disease mitigation and control
- Nonpharmaceutical efforts to minimize nosocomial spread of infectious diseases are critically important, especially in busy labor and delivery units with its inherent risks of exposure to numerous body fluids
- Clinical flexibility for facilities management is an important principle when dealing with a serious infectious disease with high potential for local spread among patients and health care providers

Influenza virus

- Even when predicted, expected, or both, emerging and reemerging infectious diseases (pandemic influenza) can cause significant morbidity and mortality in pregnancy
- Timely availability and use of influenza vaccine in pregnancy is a major priority for obstetric providers to recommend both in seasonal and pandemic outbreaks
- Influenza can be a severe respiratory disease that can be transmitted person to person before symptom onset, complicating mitigation efforts
- Early use of anti-influenza antivirals are very important and may lessen the severity of infection for mothers and their offspring
- Immediately postpartum women (2 weeks) are at similar heightened risk of morbidity and mortality as pregnant women from influenza

Ebola virus

- Pregnant women are susceptible to serious illness and death from Ebola infection
- Very high associated pregnancy wastage rates, and no infant has survived long-term after being born to an Ebola-infected mother
- Transmission of Ebola is very permissive making screening, recognition, and sequestering or cohorting* critically important interventions to undertake in the management of this infection to minimize spread
- Numerous body fluids have been found to carry Ebola infectious particles challenging infection control practices, including amniotic fluid
- Labor and delivery with its high risk of exposure to bodily fluids is a highly vulnerable area for inadvertent transmission and should be managed accordingly

Zika virus

- Unexpected new or reemerging infections can arise at any time, from any location, and can threaten the entire global health community
- The combination of the exact nature of transmission and the effect of an emerging infectious disease drives the societal attention and medical establishment's response in real time
- When little substantiated data are available at the onset of outbreaks, more conservative public health guidance is appropriately delivered
- Public health guidance must be appropriately updated, altered, or both as the nature and understanding of a novel outbreak evolves
- The true and full effect of outbreaks with teratogenic potential is not known for many years after the outbreak ensues

SARS, severe acute respiratory syndrome.
*Cohorting is grouping of persons (patients or health care workers) who have been exposed to a disease—a form of isolating groups to minimize disease spread within in location.

patients, and health care facilities from this particular outbreak are highlighted in Box 2.

INFLUENZA VIRUS

Influenza is a well-recognized cause of recurrent yearly global epidemics of febrile respiratory disease and has been documented as such for at least the previous four centuries. During this time, records suggest that the global community has experienced at least 30 influenza pandemics. The most severe recorded influenza pandemic was the 1918–1919 Spanish flu with estimates of global mortality of at least 20 million.[6,7] More recently the global community endured the 2009 H1N1 influenza pandemic and its associated morbidity and mortality, mostly noted in adults younger than 50 years of age, including disproportionate numbers of pregnant and puerperal women. The natural history of influenza mutation combined with the inevitability of antigenic shift (producing pandemic strains) makes influenza an emerging pathogen of interest.[6,7]

Influenza infection is primarily transmitted person to person through large droplets generated by coughing and sneezing from an already infected (and often asymptomatically incubating) person. In addition to respiratory droplets, transmission is also possible by contact, either directly to a susceptible host or by passive transfer through an intermediate object (ie, contaminated hands or objects). The incubation period for influenza is approximately 1–4 days followed by acute onset of fever, chills, nonproductive cough, nasal

congestion, headache, sore throat, malaise, and fatigue. Most patients have a combination of systemic symptoms and respiratory symptoms, and this finding can help differentiate influenza from other common respiratory pathogens. However, influenza is primarily a respiratory disease and most associated serious morbidity and mortality are attributable to respiratory compromise. Importantly, patients are infectious and transmit the virus during the short incubation period before symptom onset. This fact explains some of the challenges with prevention of spread in the population and in facilities.[6]

The occurrence of an upcoming influenza pandemic was well-predicted and expected (based mostly on the time lapse since the last flu pandemic). However, the source, timing, and location of the outbreak were not predicted and provided some early challenges for a global response.[13,14,21,22] Previous 20th century influenza pandemics consistently demonstrated that pregnant women suffered from disproportionate morbidity, high rates of pregnancy wastage, and higher rates maternal mortality (when compared with the general adult population).[6,13,14] This same phenomenon was again noted during the 2009 H1N1 pandemic. Multiple publications demonstrate higher rates of morbidity, critical care admission, preterm labor and birth, and higher rates of death (approximately 5-fold to 20-fold higher than expected from population-based data) among pregnant and early postpartum women.[21–27] Although this experience was not surprising, it provides a sober reminder of the uniquely susceptible nature of pregnant and early postpartum women to severe respiratory viral infections. Moreover, this recent experience clearly reinforced the importance of influenza vaccines and the use of other therapeutic measures during pregnancy.

In this author's opinion, a beneficial and long-lasting effect of the 2009 H1N1 influenza pandemic (notwithstanding its occasionally devastating effects on pregnant women) was that the unique nature of pregnant women was elevated to an international level of recognition never noted before. Coincidental to the 2009 H1N1 pandemic was a contemporaneous publication demonstrating in a randomized controlled fashion that immunization of pregnant mothers against influenza can also provide neonatal protection against influenza for up to 6 months of life.[28] This key finding, which has been replicated in subsequent investigations coupled with additional publications highlighting the higher rates of untoward outcomes from 2009 H1N1 among pregnant women, provided a renewed scientific and policy focus on the potential for disease prevention for mothers and infants through maternal immunization.[29] This focus continues today and provides novel opportunities with new vaccine products designed specifically for use in pregnancy to minimize the maternal and neonatal infectious disease burden.

No less important was novel clinical observational data demonstrating that the use of oseltamivir in pregnancy appears to mitigate to some extent the severity of infection. These data that had previously been noted in the general population were now validated in pregnancy and justify the use of antivirals early in cases of suspected or proven influenza infection. Creanga et al showed that severity of illness among pregnant women in New York City and timing of antiviral treatment are correlated. Pregnant patients who started therapy beyond the 48-hour (after symptom onset) recommended window of treatment were more likely to have severe influenza illness (3% compared with as high as 44% having severe illness, comparing less than 48-hour to greater than 5-day treatment onset, respectively, $P=.002$).[26] Similarly, a separate larger domestic investigation of 788 pregnant women with 2009 H1N1 demonstrated a significantly elevated relative risk of 6.0 (95% confidence interval 3.5–10.6) for admission to the intensive care unit for women treated more than 4 days after symptom onset (compared with less than 48 hours).[22] Combining the limited ability to predict which pregnant women will rapidly decompensate with the fact that severe outcomes are more likely, universal early oseltamivir treatment should be given by obstetric health care providers in all clinical settings as recommended.[30]

The other important phenomenon that the 2009 H1N1 influenza pandemic demonstrated was that despite significant efforts toward preparedness, the production and distribution capabilities of the vaccine industry did not optimally match the timeline of need (ie, early in the outbreak). Optimal protection from a mass vaccination program occurs when the vaccine is given at least 2 weeks before peak population exposure risk. Despite progress made in terms of vaccine manufacturing and timeliness in the lead-up to the pandemic, the majority of vaccines became available during or after the most significant wave of infection in the fall of 2009.[31] This situation continues to stimulate alternative methods for mass vaccine production and administration that may mitigate the supply–demand mismatch in future influenza pandemics. Important lessons learned from the 2009 H1N1 experience are highlighted in Box 2.

EBOLA VIRUS

Ebola virus has been recognized as a severe viral pathogen responsible for viral hemorrhagic fever for

approximately 40 years. The strain responsible for the most recent outbreak was first identified in 1976 along the Ebola River in what is now the Democratic Republic of Congo during a local outbreak of viral hemorrhagic fever. It is another zoonotic infection that humans most commonly initially contract from the natural reservoir of fruit bats. Once established in humans, subsequent infection is transmitted very efficiently from person to person by direct contact of mucous membranes or skin with bodily fluids or contaminated objects. Sexual transmission may occur. Incubation is typically 7–10 days and humans become infectious once fever and other nonspecific symptoms ensue. After the onset of generalized manifestations, severe gastrointestinal symptoms become apparent. Given the viruses' predilection for cytokine dysregulation, progression to multiorgan failure and hemorrhagic shock commonly occurs. Case fatality rates range from 55–90%, demonstrating its aggressive nature. This is also partly the result of the lack of Ebola-specific therapy, leaving supportive care as the option.[15]

The recent Ebola virus outbreak in regions of West Africa that started in 2014 and continued into 2015 was the largest ever recorded with a total of 28,652 cases, 15,261 of which were laboratory-confirmed, and a total of 11,325 deaths (40–75% case fatality rate).[32] The WHO declared this outbreak an International Public Health Emergency on August 8, 2014, and the outbreak continued for many months thereafter. It is worth noting that few pathogens have the ability to undergo widespread dissemination like Ebola and also carry such a high mortality rate. The overwhelming majority of cases were in the West African countries of Guinea, Sierra Leone, Liberia, and Nigeria. However, there were health care worker-associated cases (as a result of travel from Western Africa) in a handful of Western countries, including the United States, which prompted significant domestic efforts toward management of the potential for exposed and infected patients arriving in Western health care facilities. Many will remember significant domestic efforts in the fall of 2014 in response to a missed opportunity for identification and containment. Although the outbreak situation has mostly resolved, the CDC keeps a small force of roughly 75 workers in affected regions to have capabilities to detect and mitigate any potential new or smoldering outbreaks.

The interface between Ebola virus infection and pregnancy was partially appreciated at the outset of the recent outbreak. Historically women have been more likely to contract Ebola infection compared with men, likely related to cultural practices and caregiver roles. No data exist to suggest that pregnancy affects susceptibility to infection. However, historical reports suggest that pregnant women are more likely to suffer worse clinical disease and succumb to illness. The two largest case series reported before the recent epidemic note a cumulative mortality in excess of 90% during pregnancy from Ebola.[33,34] Affected pregnant women were equally represented across all gestational ages and presented with similar symptoms as the nonpregnant population with the notable exception of near universal reports of hemorrhage (mostly genital tract). No differences in clinical presentation or course of disease based on age or parity were documented. Additionally, very high rates of spontaneous miscarriage (approximately 60–70%) and pregnancy-related hemorrhage (both during delivery and abortion) were noted as well as the fact that no neonates born to infected mothers have survived longer than 3 weeks.[15,34,35] Interestingly, recent data demonstrate the presence of Ebola virus RNA in amniotic fluid, cord blood, and the placenta after delivery with associated implications.[35] Overall, the recent epidemic substantiates the earlier findings of higher risk for morbidity and mortality in pregnancy. An additional trend recently noted suggests that the overall decline in regional health care workers during the 2014–2015 Ebola outbreak plus a reluctance to care for infected pregnant women (presumably as a result of gravid women's high infectivity at the delivery) may have disproportionately predisposed pregnant women to receive less overall supportive care, leading to worse outcomes.[36,37] The full extent to which these trends may have affected outcomes remains to be fully realized.

Data from the most recent 2014 outbreak also provide additional relevant information for perinatal health for obstetric health care providers to understand. The recent outbreak verifies that vertical transmission of maternal Ebola virus infection to the fetus can occur during an acute Ebola infection, subsequently leading to intrauterine fetal death, stillbirth, or neonatal death.[37] Importantly, Ebola virus has been found in the breast milk during acute disease and may have led to infection in one infant, suggesting vertical transmissibility during lactation. Ebola also persists in many body sites for months, including semen, raising concerns about persistent vertical and sexual transmission months after clinical recovery.[37] This has large implications for proper infection control practices during future outbreaks. Additional take-home concepts from the recent Ebola virus outbreak are elaborated in Box 2.

ZIKA VIRUS

The ongoing Zika virus pandemic, with its documented association with fetal anomalies and other adverse neonatal and adult neurologic morbidities, has captured the world's attention over the past 12–18 months. Modern society has not experienced a teratogenic viral outbreak since the Rubella epidemic in the 1960s.[38] A vague, poorly appreciated and understood single-stranded RNA virus, Zika was first recognized in the 1940s in Africa and has until recently been associated with sporadic small regional outbreaks of minimal global importance.[39] This most recent epidemic with its epicenter in Brazil and associated effects on fetuses has awoken the global public health community to potential devastation from a novel emerging infectious disease. Attention must not fade as we learn more about the specific implications of Zika infection in pregnancy and the virus establishes natural endemicity.[40]

Zika is primarily a mosquito-borne infection and is a member of the same family of Flaviviruses as Dengue, Chikungunya, and Yellow fever. The most common vector for transmission is the *Aedes aegypti* mosquito (similar to other flaviviruses) with *Aedes albopictus* also able to transmit. Most patients infected with Zika are unaware of the infection (asymptomatic in approximately 75% of cases); if they are symptomatic, the clinical illness is invariably mild and self-limited. Clinical reports suggest a nonspecific constellation of fever, conjunctivitis, arthralgias, and maculopapular rash with the illness typically lasting 1 week or less. Associated nonspecific symptoms such as headache, myalgias, pruritus, and vomiting are also reported and share a self-limited nature. Additionally, Zika virus has been associated with Guillain-Barré syndrome and it appears previous infection confers lifelong immunity.[39]

In addition to the primary mode of vector-borne transmission, additional forms of transmission include sexual, laboratory, and likely bloodborne (through transfusion). The combination of vector-borne and sexual transmission makes this scenario unprecedented; never before has a documented teratogen been noted to be transmitted in this combined fashion. Furthermore, this combination generates a multitude of public and sexual health issues and questions. In April 2016, then-director of the CDC Dr. Thomas Frieden noted, "Never before in history has there been a situation where a bite from a mosquito could result in a devastating malformation."[41] This situation has generated much discussion about outbreak management, containment, and improved fetal outcomes. Additionally, considerations around how to appropriately design investigations and expeditiously license pharmaceuticals and vaccinations for mitigation against this outbreak have received significant attention.[41,42]

The most striking congenital finding garnering global attention is the atypically high numbers of neonates born with microcephaly across regions in Brazil noted to have had high numbers of cases of Zika. The disease outbreak was originally noted in the spring of 2015, and early reports of higher numbers of microcephalic neonates began to accumulate late in the fall of 2015. In February 2016, the WHO declared the Zika outbreak a public health emergency of international concern.[39,41] The constellation of findings that is now being coalesced into being referred to as the "congenital Zika syndrome" includes, but is not limited to, severe microcephaly with a partially collapsed skull; thin cerebral cortices; macular scarring and retinal mottling; congenital contractures; and marked early hypertonia with associated symptoms of extrapyramidal involvement.[43] Additionally, given Zika's predilection for neural tissue, some have postulated the high potential for adverse neurodevelopmental outcomes among neonates with both overt and unrecognized Zika exposure throughout gestation.[39,43]

Currently there are no medical countermeasures available to prevent, mitigate, or manage active Zika infection. Indeed, numerous trials of various vaccine candidates are underway within academia, the pharmaceutical industry, and the National Institutes of Health.[44] Although there are promising candidates in early-stage trials, it is unlikely that a vaccine product will be available on a wide-scale basis for use among reproductive-aged women (likely target population for first use) in the near future, even with the accelerated efforts underway. Until such a product exists, the bulk of the management centers on education of prospective patients as well as obstetric health care providers about 1) the specific recommendations surrounding travel restrictions to Zika-affected areas (an ever-increasing geographic list), 2) sexual activity considerations to minimize or eliminate the possibility of exposure of both men and women, and 3) minimizing risks for mosquito bites occurring in areas with active Zika transmission. These specific recommendations, areas with travel advisories, and specifics in regard to methodology of testing for Zika infection are well delineated on both the CDC's and the College's websites, and the reader is referred to these locations for a comprehensive discussion.[45,46] A brief summary of high-level recommendations for the obstetric community is detailed in Box 3. Importantly, the CDC has also developed two pregnancy registries for women

Box 3. Zika Virus–Specific Obstetric Guidance

Identification of areas with active Zika transmission (ie, risk for mosquito-borne acquisition)

- Centers for Disease Control and Prevention website: https://www.cdc.gov/zika/geo/active-countries.html
- World Health Organization website: http://www.who.int/emergencies/zika-virus/situation-report/en/
  - The precise locations of risk for traveler-associated (or endemic or both) Zika acquisition continue to evolve
  - When possible, avoid travel to these areas when pregnant or contemplating conception

Sexual activity after travel to Zika-affected areas

- Women should avoid conception for 2 mo after returning from area with active Zika transmission
- Men should abstain from sex, practice safe sex, or both for 6 mo after returning from an area with active Zika transmission
- More information can be found at: https://www.cdc.gov/zika/prevention/protect-yourself-during-sex.html

Prevention of mosquito-borne acquisition in areas with local transmission

- Use all available measures to avoid mosquito bites
  - Use insect repellent (DEET or other U.S. Food and Drug Administration–approved repellent)—safe in pregnancy at recommended levels
  - Stay in facilities with air conditioning or that have screens on windows
  - Wear clothes that cover limbs thoroughly when outside
  - Empty all areas of standing water nearby
  - More information found at: https://www.cdc.gov/zika/prevention/prevent-mosquito-bites.html

Sexual transmission prevention

- Guidance for prevention:
  - Abstinence while pregnant if partner potentially or confirmed to be infected
  - Consistent and correct use of condoms with each sex act
  - No sex toy sharing with someone with or at risk for Zika virus
  - If the clinical scenario is consistent with Zika infection, abstain from sexual activity
  - More information can be found at: https://www.cdc.gov/zika/transmission/sexual-transmission.html

Testing specifics

- Current guidance:
  - Test those at epidemiologic risk (travel, sexual, occupational), with symptoms, or both consistent with Zika infection
  - Currently available tests are serology (antibody) as well as molecular (RNA)-based—algorithm-based, depending on time since exposure, presence, or both of symptoms
  - Consultation with local, regional, and state health departments currently recommended for testing guidance, standardization, and epidemiologic purposes
  - Commercial laboratory options currently under development
  - Further information can be found at: https://www.cdc.gov/zika/symptoms/diagnosis.html, http://www.acog.org/About-ACOG/ACOG-Departments/Zika-Virus, and http://www.who.int/csr/resources/publications/zika/laboratory-testing/en/

Obstetric management of suspected or confirmed Zika virus infection in pregnancy

- If Zika infection confirmed or strongly presumed in pregnancy:
  - Serial ultrasonogram (every 3–4 wk) in second and third trimesters to detect Zika-specific findings
  - Amniocentesis should be considered on a case-by-case basis
  - Extensive guidance with confirmed algorithms available at: http://www.acog.org/About-ACOG/News-Room/Practice-Advisories/Practice-Advisory-Interim-Guidance-for-Care-of-Obstetric-Patients-During-a-Zika-Virus-Outbreak#clinicalmanagement
  - Postnatal management should be coordinated with pediatricians; further guidance available at: https://www.cdc.gov/mmwr/volumes/65/wr/mm6533e2.htm?s_cid=mm6533e2_w

infected with Zika in the United States and in Puerto Rico.[47,48] As these valuable registries prospectively collect data, they will continue to inform the obstetric and neonatal communities on evolving Zika specifics. This outbreak continues to unfold and reminds the medical and global communities of the persistent threat of emerging infectious diseases and the unpredictable effects and human toll they can impart.

PREPAREDNESS FOR EMERGING INFECTIOUS DISEASE OUTBREAKS

The certainty of future emerging outbreaks combined with the uncertainty of the specific nature of the outbreak

makes broad preparedness measures appropriate to undertake at all levels (international, domestic, regional, and facility-specific). Much attention was noted in this regard in preparation for the last influenza pandemic for both the general population and pregnant women.[13,14,49] Many efforts were influenza-specific because the natural history of influenza evolution predicts that pandemic strains will continue to emerge.[6] However, much of the preparatory efforts also apply to other less predictable outbreaks of variable nature.[50] After the World Trade Center and Anthrax attacks in 2001, the SARS epidemic in 2003 combined with the lead-up to an impending influenza pandemic, the Pandemic and All Hazards Preparedness Act was passed in 2006 by the U.S. Congress to allow for wide-scale preparedness activities across the Department of Health and Human Services. The stated purpose of the act is "to improve the Nation's public health and medical preparedness and response capabilities for emergencies, whether deliberate, accidental, or natural."[51] In addition to other activities, the act also established a new Assistant Secretary for Preparedness and Response; provides new authorities for a number of programs, including the advanced development of medical countermeasures; and also calls for a quadrennial National Health Security Strategy.[51] The U.S. Congress reauthorized this act most recently in 2013, given the certainty of emerging infectious disease outbreaks and other unpredictable disasters and the need for preparedness planning.[51,52]

In a similar fashion, all health care facilities are encouraged (and in some respects compelled) to continually prepare for impending disasters, either manmade or natural. Facilities are obligated to have regularly updated guides to disaster management with plans for topics including (but not limited to) surge capacity management, supply chain management, evacuation planning, utilities limitations and outage management, staffing plans for use during disasters, and financial sustenance considerations. Many facilities (both general medical and maternity-specific) as well as the College and the CDC also have considered plans and issued guidance for the ethical delineation of care and triage of limited resources.[53–56] These are necessary measures for all facilities to undertake in advance of future emerging disaster scenarios given the challenge of real-time management. Proactive considerations are especially important for facilities providing obstetric care given the nuanced specifics of maternal–newborn care and because these populations are often not considered in national preparedness deliberations. Individual institutions are strongly encouraged to consider the specific challenges and solutions to assure safe and effective operations during outbreaks. Box 4 lists some maternity-specific considerations for health care providers and facilities in preparation for future emerging infectious disease outbreaks.

Box 4. Specific Measures to Consider for Obstetric Hospital Preparedness

First-order priorities

- Comprehensive and realistic planning for surge capacity
- Cohorting* plan to minimize nosocomial disease spread
- Plans for maintaining and augmenting the workforce, assuming workforce absenteeism
- Planning for continued integrity of internal and external communications
- Coordination with neonatal service for maternal–infant dyad care postpartum—consideration of alternative locations

Second-order priorities

- Improving hospital surveillance capabilities to enable appropriate patient cohorting
- Delineate schema for the ethical allocation of limited health care resources
- Preparedness education and training and drilling activities
- Expansion of on-site occupational health capabilities
- System to proactively stock necessary supplies

*Cohorting is grouping of persons (patients or health care workers) who have been exposed to a disease, a form of isolating groups to minimize disease spread within a location.

DISCUSSION

Emerging infectious diseases present constant and nuanced threats to maternal and child health internationally. Given the predisposition for many infectious diseases to place pregnant women and their offspring at higher risk for untoward outcomes, the obstetric community has specific responsibilities to optimize maternal–fetal health. Much has been learned from recent outbreaks and their implications for maternal–child health. These lessons will continue to be relevant for all current and future emerging outbreaks, wherever they may originate and whatever toll they may impart.

REFERENCES

1. Centers for Disease Control and Prevention. Emerging infectious diseases. Available at: http://wwwnc.cdc.gov/eid/page/background-goals. Retrieved November 15, 2016.
2. Institute of Medicine. Emerging infections: microbial threats to health in the United States. Washington, DC: National Academies Press; 1992.

GREG WALDEN, OREGON
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FIFTEENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515–6115
Majority (202) 225–2927
Minority (202) 225–3641

June 19, 2017

Dr. Timothy Persons
Chief Scientist
U.S. Government Accountability Office
441 G Street, N.W.
Washington, DC 20226

Dear Dr. Persons:

Thank you for appearing before the Subcommittee on Oversight and Investigations on Tuesday, May 23, 2017, to testify at the hearing entitled "U.S. Public Health Response to the Zika Virus: Continuing Challenges."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on Wednesday, June 14, 2017. Your responses should be mailed to Ali Fulling, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, DC 20515 and e-mailed in Word format to Ali.Fulling@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Tim Murphy
Chairman
Subcommittee on Oversight and Investigations

cc: The Honorable Diana DeGette, Ranking Member, Subcommittee on Oversight and Investigations

Attachment

GAO U.S. GOVERNMENT ACCOUNTABILITY OFFICE
441 G St. N.W.
Washington, DC 20548

June 29, 2017

The Honorable Tim Murphy
Chairman
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
House of Representatives

Subject: Zika Virus Response – GAO Response to Questions for the Record

This letter notifies you of our enclosed responses to questions for the record, following the May 23, 2017 hearing, "Emerging Infectious Diseases: Actions Needed to Ensure Improved Response to Zika Virus Disease Outbreaks." I am pleased to be able to provide you with the requested information. If you or your staff have any questions about our responses, please contact me at (202) 512-6412 or personst@gao.gov.

[redacted]

Timothy M. Persons, Ph.D.
Chief Scientist

Enclosure

The Honorable Tim Murphy

1. **Why does the GAO think that it is important that the FDA consolidate information about tests, and require manufacturers to list the identity of the comparator assay?**

Currently, the lack of access to performance data prevents diagnostic test users from making informed decisions about which diagnostic test to adopt or recommend during the outbreak. Information on performance characteristics presented in each diagnostic test product label was not consolidated across available tests, and the identity of the comparator assay was not listed on some labels, making it challenging for users to make informed decisions about which test to adopt or recommend to patients. As a result, recommendations on diagnostic tests in our May 2017 report encourage increased access to performance data on diagnostic tests to allow for a more informed environment for patient care (i.e., increased access to performance information for clinicians as well as a higher quality of insight in support of patient decision-making).[1]

2. **You reported that some diagnostic test users also faced challenges complying with some equipment requirements to perform specific tests. (How) has this problem been addressed, how did the costs of obtaining new equipment affect localized budgets, and can you provide some examples?**

Since our work focused on selected organizations, we are not aware of the extent to which, if any, this problem has been addressed across public health laboratories such as the Laboratory Response Network (LRN), or other laboratories at the local, state, and federal level. Even so, representatives from several public health laboratories we interviewed stated that they had to acquire specific new equipment to be able to perform a certain authorized diagnostic test and that it posed some unexpected budgetary burden upon them. For example, according to Department of Defense (DOD) officials, many DOD laboratories needed to procure the equipment required to perform the Centers for Disease Control and Prevention (CDC)'s IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA).[2] There was delayed implementation of this serological assay within DOD laboratories primarily due to the need for Army LRN participating laboratories, which constitute the majority of the DOD's LRN participating laboratories, to acquire the equipment required to perform the assay. The Army was able to secure funding for the purchase of the equipment, which was subsequently distributed down to the individual laboratories for their procurement action. As another example, a state public health laboratory we interviewed stated that they were hesitant to change to an Emergency Use Authorized test because they would have to purchase specific new equipment. CDC officials stated that the agency is working to expand diagnostic testing capacity within both public health and commercial laboratories in the United States.

The Honorable Kathy Castor

1. **Please provide an update on vaccine development and clinical trials.**

---

[1]GAO. *Emerging Infectious Diseases: Actions Needed to Address the Challenges of Responding to Zika Virus Disease Outbreaks*, GAO-17-445 (Washington, D.C.: May 23, 2017).

[2]The MAC-ELISA is used to detect antibodies created against the Zika virus. ELISA is a technique designed for detecting and quantifying substances such as antibodies. Antibodies are made by the body in response to antigens such as viruses.

At present no vaccine has been approved by the Food and Drug Administration to prevent Zika virus disease but there are several vaccines that are in different development phases. For instance, according to National Institutes of Health (NIH) officials, the National Institute for Allergy and Infectious Diseases (NIAID) is developing and investigating multiple Zika vaccine candidates, including vaccines based on technologies that have shown promise against other related diseases.[3] One candidate Zika vaccine entered a Phase 1 clinical trial in 2016. According to officials, NIAID launched a multi-site Phase 2a/2b clinical trial of this vaccine in March 2017 that aims to enroll at least 2,490 healthy participants in various sites in the Americas. The study will evaluate whether the experimental vaccine is safe and able to stimulate an adequate immune response, and importantly whether it can prevent disease in areas with ongoing mosquito-borne Zika transmission. NIAID scientists also are developing other Zika vaccine candidates using a variety of approaches that are anticipated to start clinical trials in late 2017 and 2018. According to NIAID officials, while multiple vaccine approaches are promising, it is important to realize that the development of investigational vaccines and the clinical testing required to establish their safety and effectiveness take time and a safe, effective, and fully licensed Zika vaccine likely will not be available for several years.

2. **Please provide the latest information on the Zika vaccine licensing agreement between the U.S. Army and Sanofi and any relevant details.**

We have not conducted the work necessary to answer this question. The U.S. Army should be able to provide an up-to-date answer on this inquiry.

3. **With many members of Congress, states and public health advocates worried that the Zika vaccine being developed at Walter Reed Army Institute of Research with taxpayer dollars will be priced too high, how is the federal government working to ensure Sanofi, when/if a licensing agreement is made, will sell this taxpayer funded vaccine at an affordable price to federal and state governments and to consumers?**

We have not conducted the work necessary to answer this question. The U.S. Army should be able to provide an up-to-date answer on this inquiry.

4. **How has public health advice regarding Zika evolved over the past few years for young men and women? What do we know now that we did not before and what new information could be on the horizon?**

Since the Zika virus was a newly emerging infectious disease threat in the United States relatively little was known about the virus prior to 2016. There was a lack of knowledge of Zika virus biology and infections, especially at the beginning of the U.S. outbreak. In January 2016, the Centers for Disease Control and Prevention (CDC) released interim guidelines for pregnant women that recommended that all pregnant women consider postponing travel to areas where Zika virus transmission is ongoing, and pregnant women with a history of travel to an area of Zika virus transmission should be evaluated for Zika virus infection.[4] In February 2016, the CDC

[3]Anthony Fauci, Director, National Institute of Allergy and Infectious Diseases, *Research Conducted and Supported by the National Institutes of Health (NIH) in Addressing Zika Virus Disease*, testimony before the House Committee on Energy and Commerce Subcommittee on Oversight and Investigations, May 23, 2017.

[4]E. E. Petersen, J. E. Staples, D. Meaney-Delman, *et al.* "Interim Guidelines for Pregnant Women During a Zika Virus Outbreak — United States, 2016." *Morbidity and Mortality Weekly Report,* vol. 65, no. 2 (2016):30–33.

also published guidelines for sexual transmission that recommended that men who reside in or have traveled to areas with active Zika virus transmission with pregnant partners should abstain from sexual activity or use condoms for the duration of the pregnancy.[5] For men with partners that are not pregnant CDC recommended taking several factors into account but did not suggest a timeframe that Zika virus may persist in the semen. CDC updated guidance in April 2016, stated that women with possible Zika virus exposure are recommended to wait to conceive until at least 8 weeks after symptom onset (if symptomatic) or last possible Zika virus exposure (if asymptomatic).[6] Based on new data, CDC updated guidance in September 2016 recommending that all men with possible Zika virus exposure who are considering attempting conception with their partner, regardless of symptom status, wait to conceive until at least 6 months after symptom onset (if symptomatic) or last possible Zika virus exposure (if asymptomatic).[7]

At the beginning of the outbreak, there was uncertainty regarding, which sample type to use for diagnostic testing. For instance, the Zika virus had been found to be present longer in urine than in serum or plasma, but information on just how long the virus could persist in different bodily fluids was still evolving. We now know that compared to related viruses, the Zika virus is present at low levels in bodily fluids of patients during an active infection. Information is still evolving about antigens that are unique to the Zika virus and how long the virus persists in various bodily fluids, making it difficult to develop diagnostic tests for the virus.

Knowledge about Zika virus has increased in the past year, including information about Zika virus disease incidence and distribution of cases and its associated adverse health outcomes. For example, researchers have concluded that a causal relationship exists between prenatal Zika virus infection and microcephaly and other serious brain abnormalities. While much has been learned about the Zika virus, many unknowns still remain in regards to its epidemiology, including the total number of infections, the biological mechanisms, risks, reasons for geographic differences, the full spectrum of outcomes associated with maternal-fetal transmission, the presence and duration of the virus in different bodily fluids, the role of prior Zika virus infections or exposure to other related flaviviruses, and the full spectrum of short and long-term outcomes of Zika virus infection.

5. **When does each federal agency believe they will run out of money to respond properly to Zika, including vector control, surveillance, vaccine and diagnostics development/improvement and research?**

We have not conducted the work necessary to answer this question but the Zika supplemental appropriation funds provided for in the Zika Response and Preparedness Appropriations Act, 2016 (Pub. L. No. 114-223, div. B) must be obligated by the end of the Fiscal Year 2017 (i.e., September 30, 2017). The Act also includes a provision that GAO conduct oversight of the activities supported with funds appropriated by the Act, which we have begun.

---

[5]A. M. Oster, J. T. Brooks, J. E. Stryker, *et al.* "Interim Guidelines for Prevention of Sexual Transmission of Zika Virus — United States, 2016." *Morbidity and Mortality Weekly Report,* vol. 65, no. 5 (2016):120–121.

[6]E. E. Petersen, K. N. D. Polen, D. Meaney-Delman, *et al.* "Update: Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women of Reproductive Age with Possible Zika Virus Exposure — United States, 2016." *Morbidity and Mortality Weekly Report,* vol. 65, no. 5 (2016):315–322.

[7]E. E. Petersen, D. Meaney-Delman, R. Neblett-Fanfair, *et al.* "Update: Interim Guidance for Preconception Counseling and Prevention of Sexual Transmission of Zika Virus for Persons with Possible Zika Virus Exposure — United States, September 2016." *Morbidity and Mortality Weekly Report,* vo. 65, no. 39 (2016):1077-1081.

GREG WALDEN, OREGON
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FIFTEENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE

2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515–6115
Majority (202) 225-2927
Minority (202) 225-3641

June 19, 2017

Dr. Lyle R. Petersen
Director, Division of Vector-Borne Diseases
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention
1600 Clifton Road
Atlanta, GA 30329

Dear Dr. Petersen:

Thank you for appearing before the Subcommittee on Oversight and Investigations on Tuesday, May 23, 2017, to testify at the hearing entitled "U.S. Public Health Response to the Zika Virus: Continuing Challenges."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on Wednesday, June 14, 2017. Your responses should be mailed to Ali Fulling, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, DC 20515 and e-mailed in Word format to Ali.Fulling@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Tim Murphy
Chairman
Subcommittee on Oversight and Investigations

cc: The Honorable Diana DeGette, Ranking Member, Subcommittee on Oversight and Investigations

Attachment

Committee on Energy and Commerce
Subcommittee on Oversight and Investigations
Hearing: "U.S. Public Health Response to the Zika Virus: Continuing the Challenge"
May 23, 2017

Questions for the Record for Dr. Lyle R. Petersen, Director,
Division of Vector-Borne Diseases
National Center for Emerging and Zoonotic Infectious Diseases
Center for Disease Control and Prevention

The Honorable Tim Murphy

1. How many facilities in the United States can perform the various Zika diagnostic tests?

   There are three laboratory tests used for Zika: 1) a nucleic acid-based test (NAT), which are performed on acceptable specimens including human serum, plasma, blood, or urine collected during the first two weeks after symptom onset to detect Zika; 2) serological test (e.g., IgM), which detects Zika antibodies within 2 to 12 weeks of exposure; and 3) the PRNT test, which is used for the qualitative detection of Zika virus IgM antibodies to confirm the findings of the IgM test. Forty-nine states, Puerto Rico, and Guam are able to perform the NAT test developed by CDC (Trioplex Real-time RT-PCR Assay). Forty-six states and Puerto Rico are able to perform the IgM test developed by CDC (Zika Mac-ELISA). Two CDC laboratories and six state public health laboratories in California, Florida, Maryland, Massachusetts, Michigan, and New York can perform PRNT testing. Four of these state labs (Massachusetts, Michigan, California, and New York) have agreed to serve as reference labs for other states that do not have the capability to perform the PRNT test. Commercial testing for both NAT and IgM assays is also available in all 50 states.

   a. What steps is the CDC taking to disseminate these tests, particularly the PRNT test, more widely?

      For the PRNT test, individual laboratories are responsible for developing and validating their own PRNT protocols, and CDC does not distribute, oversee, or approve PRNT testing in non-CDC laboratories. CDC does provide technical assistance upon request to laboratories seeking to implement PRNT testing.

   b. How many PRNT tests can the CDC process in one day?

      CDC laboratories can perform up to approximately 600 PRNT tests per week. The PRNT test is a multi-day, multi-step test. The turn-around time for a test result may range from 14 to 22 days.

   c. How do you plan to ramp up your capacity to process Zika diagnostic tests, in particular the PRNT test, in the coming months?

      If additional testing capacity is needed, CDC has plans in place to increase the number of tests performed at its laboratories each week to 1,000. In addition, the four reference labs

mentioned above are available to conduct PRNT testing on behalf of other states, if the need exceeds CDC's testing capacity. These four PRNT reference laboratories have agreed to perform this service through September 2017 with current emergency response funding.

2. The PRNT test is considered the "gold standard" but is not scientifically proven. How can something be considered the "gold standard" when it has not been scientifically proven?

PRNT is a well-recognized, established, and standard laboratory technique that is used to confirm the IgM test by testing for the presence of Zika antibodies. Due to cross-reaction with other flaviviruses such as dengue or chikungunya, results from other testing methods may be difficult to interpret, therefore, presumed positive, equivocal, or inconclusive tests must be forwarded for confirmation by the PRNT. CDC will continue to invest in improving the test, in accordance with available resources.

3. How many pregnant women with Zika infections have been accounted for in the United States?

As of May 23, 2017, there were 1,883 pregnant women with laboratory evidence of possible Zika virus infection in the United States and the District of Columbia. In the U.S. Territories of Puerto Rico, American Samoa and the U.S. Virgin Islands, there have been 3,916 pregnant women with laboratory evidence of possible Zika virus infection, as of May 23, 2017.

a. How many of these women completed their pregnancy?

Of the 1,883 pregnant women with laboratory evidence of possible Zika virus infection in the United States and the District of Columbia, 1,579 women have reported completing their pregnancy, as of May 23, 2017. The number of completed pregnancies with or without birth defects include those that ended in a live birth as well as pregnancy losses.

The reported number of pregnant women with laboratory evidence of possible Zika virus infection is cumulative and includes not only women who have completed their pregnancies, but also ongoing pregnancies that have not been completed. There are some delays in reporting. For some jurisdictions, the latest total number of pregnant women with Zika are available on the individual websites for each jurisdiction. In addition, reported numbers may increase or decrease as preliminary information is clarified.

Between October 13, 2016, and May 23, 2017, CDC did not report the number of completed pregnancies or outcomes for all completed pregnancies with laboratory evidence of possible Zika virus infection in the US Territories.

b. How many of these fetuses or infants had congenital birth defects?

As of May 23, 2017, CDC was aware of 72 infants born with Zika associated birth defects and 8 women had pregnancy losses with birth defects in the United States and the District of Columbia.

The Honorable Michael Burgess, M.D.

1. What has CDC done to support the limited capacity of local public health departments through technical assistance and grants, and where has the agency found challenges in supporting local responses to the Zika epidemic? Furthermore, how does HHS plan to further support capacity building efforts in the coming months, particularly as we get into the months where we could see local transmission of Zika in the United States?

   CDC is coordinating closely with state and local partners to ensure local public health departments are equipped to prevent, respond to, and eliminate the threat of Zika virus. These actions range from regular communications to direct personnel support. Examples include:

   - Developed the Zika Interim Response Plan for use by state, territorial, local and tribal jurisdictions[1], including posting online with resources such as an epidemiologic investigation toolkit, and a communication planning guide
   - Created Zika virus testing kits, which state public health laboratories receive free of charge
   - Conducted additional testing for states that lacked sufficient capacity
   - Provided guidance on mosquito control and evaluation of mosquito control district plans and interventions, as requested
   - Created the U.S. Zika Pregnancy and Infant Registries to collect health data about pregnant women with laboratory evidence of Zika virus infection and their babies through the first year of life and created rapid Zika Birth Defects Surveillance system to identify babies born with birth defects associated with Zika regardless if their mother's Zika infection was detected during pregnancy.
   - Established Zika Care Connect [2], a network of specialty healthcare providers that connects pregnant women, parents, and caregivers of infants and families affected by Zika to specialized care
   - Placed field assignees on-site at 26 local health departments in communities with pregnant women with laboratory evidence of possible Zika virus infection through the Local Health Department Initiative
   - Deployed CDC Emergency Response Teams (CERT) to 14 different cities to support local communities in responding to Zika

   As of May 15, 2017, CDC has provided $251 million directly to state, local, and territorial health departments through grants from redirected and supplemental funding. CDC also provided $44 million in Public Health Emergency Preparedness (PHEP) reimbursement funding to states and territories in October 2016. CDC directed emergency funding to areas with the greatest need and continues to provide ongoing, in-depth support to Florida, Texas, and U.S. territories where public health officials are battling local transmission of mosquito-borne Zika.

   In addition to direct funding, CDC has awarded funding that supports state, local, and territorial efforts, including support to partner organizations, vector-borne disease regional Centers of Excellence, and the Puerto Rico Vector Control Unit. These financial resources have been

[1] Zika Interim Response Plan https://www.cdc.gov/zika/pdfs/zika-draft-interim-conus-plan.pdf

[2] Zika Care Connect - https://www.zikacareconnect.org/

coupled with technical support to states and territories through rapid response teams, as well as laboratory, epidemiologic, entomologic, field investigation, and data management support.

CDC has plans for all remaining supplemental funds, including needs that may arise with the 2017 mosquito season. The majority of remaining funds will be provided directly to state, local, and territorial health departments through the Epidemiology and Laboratory Capacity cooperative agreement for Zika activities, including epidemiology and laboratory capacity, vector surveillance and control, and the U.S. Zika Pregnancy and Infant Registries. Remaining funds will also support CDC operations, including staff, travel, rapid response teams (if needed), and laboratory supplies and equipment.

2. Last year as we began to discuss appropriating funds to support our efforts in addressing the Zika epidemic, there were discussions around the potential establishment of a new, flexible emergency preparedness fund for addressing future, emerging threats like Zika and Ebola. There are two existing revenue streams that the CDC receives that I would like to examine as potential infrastructure for developing such a fund: the Public Health Emergency Preparedness Cooperative Agreement and the Public Health Emergency Fund. Current appropriations levels aside, what flexibility has the CDC been able to wield in utilizing either of these funds, and what barriers would prevent the CDC from utilizing either of these funds in the future?

   The distribution of Public Health Emergency Preparedness (PHEP) cooperative agreement funds is calculated using a formula established under section 319C-1(h) of the Public Health Service Act. Once a PHEP award is provided to an eligible entity, an awardee may not redirect the cooperative agreement funding to a public health emergency unless the awardee requests and HHS grants approval to use PHEP funds for emergency activities that fall within the existing PHEP cooperative agreement scope of work. The majority of CDC's Zika response activities were funded through the Public Health Preparedness and Response (PHPR) Zika cooperative agreement (see: https://www.cdc.gov/phpr/readiness/funding-zika.htm).

   The Public Health Emergency Fund has not received any appropriations for a number of years. The Public Health and Social Services Emergency Fund has received appropriations, but is managed by the Department of Health and Human Services.

The Honorable Frank Pallone

1. HHS recently reported that CDC has obligated $332.2 million of its fiscal year 2017 Zika funds. How much funding does CDC have remaining for 2017 Zika preparation and response? Does CDC have sufficient funds remaining to support these efforts for the remainder of fiscal year 2017?

   As of May 15, 2017, CDC has obligated a total of $338 million of the $394 million appropriated in the Zika Response and Preparedness Act (division B of Public Law 114-223).

   CDC has plans for all remaining supplemental funds, including needs that may arise during the 2017 mosquito season. The majority of remaining funds will be provided directly to state, local, and territorial health departments through the Epidemiology and Laboratory Capacity cooperative agreement for Zika activities, including epidemiology and laboratory capacity, vector surveillance and control, and the U.S. Zika Pregnancy and Infant Registries. The rest of

the remaining funds will support CDC operations, including staff, travel, rapid response teams (if needed), and laboratory supplies and equipment.

The Honorable Kathy Castor

1. Please provide an update on vaccine development and clinical trials.

   This question is best addressed by the National Institute of Health (NIH) and Biomedical Advanced Research and Development Authority (BARDA).

2. Please provide the latest information on the Zika vaccine licensing agreement between the U.S. Army and Sanofi and any relevant details.

   Questions related to the licensing agreement between the U.S. Army and Sanofi are best addressed by the Department of Defense (DoD), Department of the Army.

3. With many members of Congress, states and public health advocates worried that the Zika vaccine being developed by the Walter Reed Army Institute of Research with taxpayer dollars will be priced too high, how is the federal government working to ensure Sanofi, when/if a licensing agreement is made, will sell this taxpayer funded vaccine at an affordable price to federal and state governments and consumers?

   This question is best addressed by the DoD, Department of the Army.

4. How has public health advice regarding Zika evolved over the past few years for young men and women? What do we know now that we did not before and what new information could be on the horizon?

   Prior to 2015, there was limited knowledge about Zika virus and no awareness of the potential effects of Zika on infants exposed to the virus during pregnancy. Zika was a newly emerging infectious disease in the Western Hemisphere and had only been seen previously in outbreaks among small populations. We have since learned that pregnant women and infants are the most vulnerable to adverse outcomes associated with Zika virus infection, including:
   - In April 2016, CDC [3] published the evidence to confirm that Zika virus is the first known mosquito-borne virus to cause birth defects in humans.
   - A CDC study [4], issued in March 2017, has demonstrated that Zika virus directly attacks the developing infant's brain, causing microcephaly and other birth defects. A distinct pattern of birth defects, called congenital Zika syndrome [5], has emerged among fetuses and infants of some women infected with Zika during pregnancy. Congenital Zika syndrome likely represents the most severe impact of congenital infection (infection acquired during pregnancy) that can be seen at birth. This syndrome includes severe microcephaly (small

[3] *The New England Journal of Medicine.* "Zika Virus and Birth Defects — Reviewing the Evidence for Causality." http://www.nejm.org/doi/full/10.1056/NEJMsr1604338?query=featured_zika
[4] *Emerging Infectious Diseases.* "Zika Virus RNA Replication and Persistence in Brain and Placental Tissue." https://wwwnc.cdc.gov/eid/article/23/3/16-1499_article
[5] *JAMA.* "Characterizing the Pattern of Anomalies in Congenital Zika Syndrome for Pediatric Clinicians." http://jamanetwork.com/journals/jamapediatrics/fullarticle/2579543

head size) resulting in a partially collapsed skull; decreased brain tissue with brain damage; damage to the eye; limited range of joint motion, such as clubfoot, and too much muscle tone restricting body movement. However, the full spectrum of poor birth outcomes caused by Zika virus infection during pregnancy remains unknown. With other congenital infections, some babies are born apparently healthy but have later onset problems such as deafness. In order to understand the full range of disabilities that might occur, it is essential to follow up with infants and children who were exposed to Zika during pregnancy until they are at least 2-3 years of age, and longer will be needed to understand the full impact of congenital Zika virus infection.

CDC has also discovered a link between Zika virus and Guillian-Barré syndrome (GBS). Current CDC research suggests that GBS is strongly associated with Zika infections; however, only a small proportion of people with recent Zika virus infection get GBS. CDC is continuing to investigate the link between GBS and Zika to learn more.

CDC has collected and communicated information to assist men, women and families in understanding 1) the risks of Zika, 2) ways to prevent Zika, 3) diagnostic methods for Zika, and 4) clinical services that may assist with the long-term consequences of Zika during pregnancy. Guidance from CDC as part of its public health response to Zika has been directly informed by several major findings gleaned from surveillance data:

1) CDC issued guidance to the American population in early 2016 to advise pregnant women and couples planning pregnancy not to travel to areas with Zika. This guidance was issued as a precautionary measure even before Zika was a proven cause of adverse outcomes, and we will never know how many families were protected from Zika as a result of this rapid action.
2) Data captured through the Zika Pregnancy and Infant Registries, newly established public health surveillance systems, provide rough estimates of the potential risk of fetal/infant birth defects associated with a maternal Zika virus infection at different timeframes during pregnancy. These data are used by healthcare providers counseling patients and are the first population-based risk estimates available.
   - In April 2017, CDC reported on data from the Zika Pregnancy and Infant Registries [6] indicating that among 1,000 pregnant women with evidence of Zika with completed pregnancies in 2016, 10 percent of those with confirmed Zika infection had babies with Zika-associated birth defects.
3) Surveillance data have shown that the risk for birth defects among infants exposed during pregnancy is the same regardless of whether an infected pregnant woman had symptoms of Zika virus. This was the first time it was determined that women without symptoms were at risk, which strengthened the current recommendations to avoid travel and to screen pregnant women for Zika virus infection.
4) In July 2016, CDC confirmed [7] that Zika virus can be sexually transmitted from person to person. This has the most profound impact on young men and women who become pregnant or are planning a pregnancy because of the risks of simultaneous sexual transmission of Zika and conception.

---

[6] *Morbidity and Mortality Weekly Report.* "Vital Signs: Update on Zika Virus–Associated Birth Defects and Evaluation of All U.S. Infants with Congenital Zika Virus Exposure — U.S. Zika Pregnancy Registry, 2016." https://www.cdc.gov/mmwr/volumes/66/wr/mm6613e1.htm

[7] *Morbidity and Mortality Weekly Report.* "Update: Interim Guidance for Prevention of Sexual Transmission of Zika Virus — United States, July 2016." https://www.cdc.gov/mmwr/volumes/65/wr/mm6529e2.htm?s_cid=mm6529e2_w

5) Surveillance data indicates that Zika virus may persist in the body longer than expected. This directly impacts recommendations for couples planning a pregnancy.
   - Current research indicates that Zika virus RNA can remain in semen up to 6 months, longer than in other body fluids, including vaginal fluids, urine, and blood.
   - Emerging data from case reports [8] of some pregnant women published in October 2016 indicates that Zika virus RNA persists in some pregnant women longer than the 1-2 weeks previously reported and may provide a window into the way the virus crosses the placenta.

Many questions remain. Among the most urgent are:

What is the full spectrum of adverse outcomes caused by Zika virus infection during pregnancy?

- CDC established the Zika Pregnancy and Infant Registries to monitor pregnancy and infant outcomes to learn more about the timing, absolute risk, and spectrum of outcomes associated with Zika virus infection during pregnancy. The surveillance effort is dependent on the collaboration of clinicians and state, tribal, local, and territorial health departments and sustained resources.

What is the best way to detect and diagnose congenital Zika virus infection?

- Much of the data about the detection and persistence of Zika virus is limited. It is unclear what the best testing paradigm is that provides a timely diagnosis and correlates with risks. In addition, the findings of Zika virus persistence requires further exploration to determine how this can help men, women and families plan for pregnancy.

What are the long-term medical and developmental outcomes for infants and children affected by congenital Zika syndrome?

- Many infants enrolled in the Zika Pregnancy and Infant Registries are now approaching one year of age, which limits the ability to study long-term effects of the disease. Information is needed by families, healthcare providers, communities, governmental organizations and others to identify needs and plan for necessary services.

- Recognizing that coordinated surveillance systems are the only way to obtain accurate information about the scope and nature of impacts of the Zika virus infection, CDC awarded funds to 45 jurisdictions to collect information about birth defects thought to be related to Zika virus infection. The surveillance system closes the gap in reporting by including infants with birth defects and congenital Zika virus exposure who may have been missed by pregnancy and infant registries if the mother's Zika infection was not detected prenatally.

5. When does each federal agency believe they will run out of money to respond properly to Zika, including vector control, surveillance, vaccine and diagnostics development/improvement and research?

   All remaining supplemental funds will be obligated by September 30, 2017. The majority of remaining funds will be provided directly to state, local, and territorial health departments through the Epidemiology Laboratory Capacity cooperative agreement for Zika activities, including

[8] *Obstetrics & Gynecology.* "Prolonged Detection of Zika Virus RNA in Pregnant Women." http://journals.lww.com/greenjournal/Pages/articleviewer.aspx?year=2016&issue=10000&article=00007&type=Fulltext

epidemiology and laboratory capacity, vector surveillance and control, and the U.S. Zika Pregnancy and Infant Registries. The rest of the remaining funds will support CDC operations, including staff, travel, rapid response teams (if needed), and laboratory supplies and equipment.

GREG WALDEN, OREGON
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FIFTEENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE

2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515–6115
Majority (202) 225-2927
Minority (202) 225-3641

June 19, 2017

Dr. Luciana Borio
Acting Chief Scientist
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Borio:

Thank you for appearing before the Subcommittee on Oversight and Investigations on Tuesday, May 23, 2017, to testify at the hearing entitled "U.S. Public Health Response to the Zika Virus: Continuing Challenges."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on Wednesday, June 14, 2017. Your responses should be mailed to Ali Fulling, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, DC 20515 and e-mailed in Word format to Ali.Fulling@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Tim Murphy
Chairman
Subcommittee on Oversight and Investigations

cc: The Honorable Diana DeGette, Ranking Member, Subcommittee on Oversight and Investigations

Attachment

U.S. FOOD & DRUG ADMINISTRATION

OCT 19 2017

The Honorable Morgan Griffith
Vice Chairman
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
House of Representatives
Washington, D.C, 20515

Dear Mr. Vice Chairman:

Thank you for providing the Food and Drug Administration (FDA or the Agency) with the opportunity to testify at the May 23, 2017, hearing before the Subcommittee on Oversight and Investigations, House Committee on Energy and Commerce, entitled "U.S. Public Health Response to the Zika Virus: Continuing Challenges." This letter is a response for the record to questions posed by the committee.

If you have further questions, please let us know.

Sincerely,

[redacted]

John M. Martin
Principal Associate Commissioner
for Legislation

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20903
www.fda.gov

We have restated your questions below in bold, followed by our responses.

The Honorable Tim Murphy

1. **Dr. Borio, the FDA revoked the authorization for one of the Zika tests. What would lead the FDA to revoke a test after just being authorized?**

FDA revoked the emergency use authorization (EUA) for the LightMix® Zika rRT-PCR Test — which was initially authorized for emergency use on August 26, 2016 — on March 13, 2017, in response to Roche Molecular Systems Inc.'s request dated March 10, 2017, to withdraw the EUA due to technical performance and business considerations.

The Honorable Frank Pallone

1. **How much funding does FDA have remaining for 2017 Zika preparation and response? Does FDA have sufficient funds remaining to support these efforts for the remainder of fiscal year 2017?**

The Zika Response and Preparedness Act (division B of Public Law 114-223) did not provide any funding to FDA for Zika response activities. To help support these activities at the start of the fiscal year, FDA used base appropriations provided by the Continuing Appropriations Act, 2017 (division C of Public Law 114-223), and reallocated $5 million of the $25 million appropriated for Ebola response activities by the Consolidated and Further Continuing Appropriations Act, 2015 (title VIII of division A of Public Law 113-235). As of May 19, 2017, FDA had obligated $1.8 million of the reallocated Ebola funding, and anticipates obligating the remaining balance by the end of FY 2017.

In May 2017, the Consolidated Appropriations Act, 2017 (title VII of division A of Public Law 115-31) provided an additional $10 million in no-year funding for FDA "to prevent, prepare for, and respond to emerging health threats, including the Ebola and Zika viruses, domestically and internationally and to develop necessary medical countermeasures and vaccines, including the review, regulation, and post market surveillance of vaccines and therapies, and for related administrative activities". This funding—in addition to FDA's base appropriations and the $5 million reallocated from appropriations for Ebola response—should provide FDA with sufficient funding to support continued Zika virus response activities in FY 2017, provided another public health emergency does not occur that would necessitate a reprioritization of funding.

The Honorable Kathy Castor

1. **Please provide an update on vaccine development and clinical trials.**

FDA is actively engaged with the National Institutes of Health (NIH) and the Biomedical Advanced Research and Development Authority (BARDA), the international community, and product developers to help accelerate vaccine development programs. However, FDA generally

cannot comment on the status of any particular vaccine development program because of confidentiality requirements. We would refer this question to NIH and BARDA.

2. **Please provide the latest information on the Zika vaccine licensing agreement between the U.S. Army and Sanofi and any relevant details.**

Questions related to the licensing agreement between the U.S. Army and Sanofi are best addressed by the Department of Defense (DoD), Department of the Army.

3. **With many members of Congress, states and public health advocates worried that the Zika vaccine being developed at the Walter Reed Army Institute of Research with taxpayer dollars will be priced too high, how is the federal government working to ensure Sanofi, when/if a licensing agreement is made, will sell this taxpayer funded vaccine at an affordable price to federal and state governments and to consumers?**

This question is best addressed by DoD, Department of the Army.

4. **How has public health advice regarding Zika evolved over the past few years for young men and women? What do we know now that we did not before and what new information could be on the horizon?**

This question is best addressed by the Centers for Disease Control and Prevention.

5. **When does each federal agency believe they will run out of money to respond properly to Zika, including vector control, surveillance, vaccine and diagnostics development/improvement and research?**

In May of 2017, the Consolidated Appropriations Act, 2017 (title VII of division A of Public Law 115-31) provided $10 million in no-year funding for FDA "to prevent, prepare for, and respond to emerging health threats, including the Ebola and Zika viruses, domestically and internationally and to develop necessary medical countermeasures and vaccines, including the review, regulation, and post market surveillance of vaccines and therapies, and for related administrative activities". FDA anticipates expending this funding from FY 2017 through FY 2019 to support preparedness and response activities. This additional funding—in addition to FDA's base appropriations—should provide FDA with sufficient funding to support continued Zika virus response activities in that timeframe, provided another public health emergency does not occur that would necessitate a reprioritization of funding.

GREG WALDEN, OREGON
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FIFTEENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515–6115
Majority (202) 225–2927
Minority (202) 225–3641

June 19, 2017

Dr. Anthony Fauci
Director, National Institute of Allergy and Infectious Diseases
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Fauci:

Thank you for appearing before the Subcommittee on Oversight and Investigations on Tuesday, May 23, 2017, to testify at the hearing entitled "U.S. Public Health Response to the Zika Virus: Continuing Challenges."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on Wednesday, June 14, 2017. Your responses should be mailed to Ali Fulling, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, DC 20515 and e-mailed in Word format to Ali.Fulling@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Tim Murphy
Chairman
Subcommittee on Oversight and Investigations

cc: The Honorable Diana DeGette, Ranking Member, Subcommittee on Oversight and Investigations

Attachment

Committee on Energy and Commerce
Subcommittee on Oversight and Investigations
Hearing: "U.S. Public Health Response to the Zika Virus: Continuing the Challenge"
May 23, 2017

Questions for the Record for Dr. Anthony Fauci, Director,
National Institute of Allergy and Infectious Diseases, National Institutes of Health

The Honorable Tim Murphy

1. What is the expected production volume for the vaccine once it is approved?

The National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), facilitates research and development of vaccine candidates, which typically includes the support of early stage clinical trials to investigate vaccine safety and efficacy. The production volume of an FDA-approved Zika vaccine would be determined by the vaccine manufacturer, and will depend in part on the licensed indications and approved usage of the vaccine in the U.S. and elsewhere.

a. Which population will be prioritized for the vaccine and why?

The initial target population for an approved Zika vaccine will likely be adults and adolescents of reproductive age, excluding pregnant women. This is the same target population as for the Phase II/IIb clinical trial testing of the NIAID Vaccine Research Center (VRC) investigational DNA vaccine.

NIAID also is supporting research on other vaccine candidates, including live-attenuated approaches that could potentially induce longer-lasting protection, possibly for decades. These vaccines might be evaluated in children, anticipating that vaccination in childhood could protect individuals through childbearing years. A strategy of childhood vaccination may be particularly effective in areas where Zika virus is endemic and there is greatest risk of congenital Zika syndrome. In the future, Zika vaccine candidates that have been found to be safe in non-pregnant populations may be investigated to determine if they are safe and effective in pregnant women.

2. Why does Zika cause microcephaly, yet other flaviviruses such as dengue, chikungunya, and yellow fever are not known to cause microcephaly?

NIAID is actively engaged in efforts to better understand the Zika virus, including any differences between Zika virus and other related flaviviruses that may help explain why Zika can cause microcephaly. For example, NIAID-supported investigators have developed animal models of Zika virus infection during pregnancy to better understand congenital Zika syndrome, which is a pattern of birth defects that includes severe microcephaly. These NIAID-funded animal studies have shown that Zika virus is capable of crossing the placental barrier and impairing fetal brain development in pregnant animals.

In addition, NIH-supported investigators have discovered that neural precursor cells, which give rise to new cells in the developing brain, have receptors that make these cells particularly vulnerable to infection by Zika virus. NIH-supported researchers are now investigating how Zika virus exploits the cellular, molecular, and biochemical pathways within these cells to propagate the virus and cause these cells to die. They also are investigating how the immune system interacts with Zika virus within the central nervous system to better understand which aspects might be enhanced to help control the virus and whether the brain's immune response to the virus might also cause collateral damage that contributes to cell death.

NIAID also is supporting research to address concerning reports of infants born to Zika virus-infected mothers that appear healthy at birth but later experience slowed head growth during the first year followed by postnatal microcephaly. NIAID is partnering with the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the National Institute of Environmental Health Sciences, and the Brazilian research institute, Fiocruz, to better understand these observations. This study, Zika in Infants and Pregnancy (ZIP), is a multi-center, international, prospective cohort study of 10,000 women in Zika-affected regions. Enrollment of women early in their pregnancy is ongoing, and their children will be followed for at least one year after birth. The information gained from this study will help improve our understanding of congenital Zika syndrome, enhance care for pregnant women and their infants, and guide interventions for affected children.

The Honorable Frank Pallone

1. HHS recently reported that NIH has obligated $68.8 million of its fiscal year 2017 Zika funds. How much funding does NIH have remaining in 2017 for Zika preparation or response? Does NIH have sufficient funds remaining to support these efforts for the remainder of fiscal year 2017?

As of May 15, 2017, the National Institute of Health (NIH) has obligated $71.36 million of the $152 million in NIH supplemental funds provided by the Zika Response and Preparedness Act 2016 (division B of Public Law 114-223). The remaining $80.64 million will be obligated by the end of FY 2017. We anticipate these funds will be sufficient to support Zika-related activities currently planned through FY 2017.

The Honorable Kathy Castor

1. Please provide an update on vaccine development and clinical trials.

A safe and effective Zika vaccine would be an invaluable tool to help stop the spread of infection and prevent future outbreaks. NIAID is developing and investigating multiple Zika vaccine candidates.

DNA-based Zika vaccine candidate: NIAID recently launched a multi-site Phase II/IIb clinical trial of the NIAID VRC's DNA-based vaccine candidate in March 2017 following positive

results in Phase I testing. This trial aims to enroll at least 2,490 healthy participants in various sites in the Americas, including the continental United States, U.S. territories, and countries in Central and South America. This Phase II/IIb study will further evaluate whether the experimental vaccine is safe and able to stimulate an adequate immune response, and importantly whether it can prevent disease in areas with ongoing mosquito-borne Zika virus transmission. The clinical trial will enroll adults and adolescents of reproductive age. Part A of the study will enroll 90 healthy men and non-pregnant women ages 18-35 years at Baylor College of Medicine (Houston, Texas) and University of Puerto Rico Medical Sciences Campus (San Juan, Puerto Rico). Part B will enroll 2,400 healthy men and non-pregnant women ages 15-35 years in these Part A sites and Brazil, Peru, Costa Rica, Panama, and Mexico. The effects of the vaccine on a developing fetus are unknown, and therefore women who are pregnant or plan to become pregnant will not be eligible for the trial. The study is expected to conclude in 2019, although the exact timing of the trial will depend on the intensity of Zika virus transmission and the efficacy of the vaccine candidate.

Zika purified inactivated vaccine (ZPIV) candidate: NIAID is collaborating with the Biomedical Advanced Research and Development Authority (BARDA) and the Walter Reed Army Institute of Research (WRAIR) to evaluate a ZPIV candidate developed by WRAIR. ZPIV is based on an approach used to develop vaccines against the related dengue and Japanese encephalitis viruses. NIAID is co-funding the Phase I clinical trials program with WRAIR. Trials testing ZPIV began in November 2016 at the WRAIR Clinical Trial Center in Silver Spring, Maryland; the Center for Virology and Vaccine Research, part of Beth Israel Deaconess Medical Center and Harvard Medical School in Boston; the Center for Vaccine Development at the Saint Louis University School of Medicine; and the clinical research center CAIMED, part of Ponce Health Sciences University in Puerto Rico. The Saint Louis University School of Medicine site is an NIAID-funded Vaccine Evaluation and Treatment Unit (VTEU) that is able to enroll large numbers of volunteers and vaccinate them in a rapid, safe, and effective manner. Having the rapid-response capability of the NIAID VTEUs in place ahead of an outbreak allows for accelerated testing of vaccines designed to address Zika virus and other emerging public health threats.

Live-attenuated Zika vaccine candidates: NIAID scientists are developing live-attenuated Zika vaccine candidates using an approach similar to that taken with an experimental vaccine against the closely related dengue virus. This vaccine candidate will enter an NIAID Phase I clinical trial in late 2017. Thereafter, this Zika-only candidate will be combined with the tetravalent dengue vaccine candidate designed to protect against all four circulating strains of dengue virus. A Phase I trial of this new pentavalent combination Zika/dengue candidate vaccine is scheduled to enter clinical testing by 2018. NIAID is working with development partners in Brazil to plan later-stage trials of this combination vaccine.

Early-stage Zika vaccine candidates: NIAID-supported researchers are evaluating investigational mRNA vaccines, which are broadly similar to DNA vaccines. The NIAID VRC and other NIAID intramural researchers are working with academic and industry partners to evaluate various mRNA vaccine technologies to identify potential candidates for further development. These include an investigational vaccine under development by the NIAID VRC and the pharmaceutical company GSK that may enter clinical trials in late 2017.

2. Please provide the latest information on the Zika vaccine licensing agreement between the U.S. Army and Sanofi and any relevant details.

The ZPIV candidate was developed by WRAIR, and NIAID is supporting Phase I clinical testing of this vaccine as described above. NIAID is not involved in the development of the Zika vaccine licensing agreement between the U.S. Army and Sanofi. You may wish to contact the Department of Defense to address any specific questions on the vaccine licensing agreement for the ZPIV candidate between the U.S. Army and Sanofi.

3. With many members of Congress, states and public health advocates worried that the Zika vaccine being developed at the Walter Reed Army Institute of Research with taxpayer dollars will be priced too high, how is the federal government working to ensure Sanofi, when/if a licensing agreement is made, will sell this taxpayer funded vaccine at an affordable price to federal and state governments and to consumers?

NIAID is not involved in the development of the Zika vaccine licensing agreement between the U.S. Army and Sanofi. You may wish to contact the Department of Defense to address any specific questions on the vaccine licensing agreement for the ZPIV candidate between the U.S. Army and Sanofi.

4. How has public health advice regarding Zika evolved over the past few years for young men and women? What do we know now that we did not before and what new information could be on the horizon?

NIAID defers to the Centers for Disease Control and Prevention to respond to this question about public health advice regarding Zika.

5. When does each federal agency believe they will run out of money to respond properly to Zika, including vector control, surveillance, vaccine and diagnostics development/ improvement and research?

The remaining NIH funds provided by the Zika Response and Preparedness Act 2016 (division B of Public Law 114-223) will be obligated by the end of FY 2017. We anticipate these funds will be sufficient to support Zika-related activities currently planned through FY 2017.

GREG WALDEN, OREGON
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FIFTEENTH CONGRESS

Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515–6115
Majority (202) 225-2927
Minority (202) 225-3641

June 19, 2017

Dr. Rick A. Bright
Director, Biomedical Advanced Research and Development Authority
Deputy Assistant Secretary, Office of the Assistant Secretary for Preparedness and Response
U.S. Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, DC 20201

Dear Dr. Bright:

Thank you for appearing before the Subcommittee on Oversight and Investigations on Tuesday, May 23, 2017, to testify at the hearing entitled "U.S. Public Health Response to the Zika Virus: Continuing Challenges."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on Wednesday, June 14, 2017. Your responses should be mailed to Ali Fulling, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, DC 20515 and e-mailed in Word format to Ali.Fulling@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Tim Murphy
Chairman
Subcommittee on Oversight and Investigations

cc: The Honorable Diana DeGette, Ranking Member, Subcommittee on Oversight and Investigations

Attachment

House of Representatives Energy and Commerce
Subcommittee on Oversight and Investigations
Hearing: "U.S. Public Health Response to the Zika Virus: Continuing Challenges"
Tuesday, May 23, 2017

Question for Dr. Rick Bright, Director, Biomedical Advanced Research and Development Authority (BARDA); Deputy Assistant Secretary, Office of the Assistant Secretary for Preparedness and Response (ASPR)

The Honorable Tim Murphy

1. What is our current capacity to test for the Zika virus in the United States?

The United States needs laboratory diagnostic tests to detect acute Zika infection and manage Zika infection in pregnant women. Active Zika infection is diagnosed using molecular assays [e.g., Polymerase Chain Reaction (PCR)] that detect Zika virus RNA in acceptable specimens including human serum, plasma, whole blood and urine. Because 80 percent of Zika infections are asymptomatic, people do not often seek medical care during the period when the Zika virus can be best detected. Serology tests (e.g., ELIA, IgM) that detect antibodies produced in response to Zika virus are used to detect Zika virus infection in people who are past the window when molecular tests are effective. HHS agencies have been working aggressively and collaboratively since early 2016 to make both molecular and serologic Zika diagnostic testing available to U.S. states, territories, and affiliated islands through public health laboratories and in clinical laboratories.

   a. In your opinion, is this capacity sufficient to meet demand for diagnostic tests, particularly among pregnant women in the summer months?

   Local transmission of Zika virus may occur this summer in parts of the United States, particularly in parts of Florida, Texas, and Hawaii that have previously experienced local transmission of dengue or chikungunya. Considering the number of molecular and serologic tests that are now readily available for clinical use (hospital, commercial laboratories) and public health laboratories, there is likely a sufficient capacity to provide Zika molecular and serologic testing. This capacity should serve the anticipated demand from pregnant women who may have been exposed to Zika, symptomatic individuals with risk of exposure in a localized outbreak, and travelers returning from Zika endemic regions.

   b. How does HHS plan to ramp up this capacity in the coming months, particularly as we get into the months where we could see local transmission of Zika in the United States?

The Zika MAC ELISA and the Trioplex rRT-PCR assays, developed by the Centers for Disease Control and Prevention (CDC), are available through the CDC Laboratory Response Network (LRN), and other public health and Department of Defense (DoD) laboratories in the United States and its territories. Both assays are provided by CDC under an Emergency Use Authorization (EUA) provided by the U.S. Food and Drug Administration (FDA).

BARDA and FDA have been working to bring commercial diagnostic tests to market, which would make testing available outside of the public health laboratory system. Eleven Zika PCR assays developed by commercial manufacturers are available under FDA EUA for use in certain private sector clinical laboratories (hospitals, large commercial laboratories). Any Clinical Laboratory Improvement Amendments (CLIA) accredited laboratory wishing to perform Zika molecular testing is able to purchase these tests from any one of eight different companies, or send their specimens to three different reference laboratories for Zika PCR testing. Due to the diverse nature of the U.S. clinical laboratory system and preferences by individual labs for different tests, it is not possible to estimate the total number of tests these laboratories can perform. Large commercial laboratories such as Quest and LabCorp generally have capacity to perform many hundreds of tests each week, and capacity to surge for additional testing demand if needed. These laboratories are equipped for rapid turn-around time and electronic reporting, which speeds up access to results from the ordering physician to the patient.

Testing for IgM antibodies to Zika is challenging due to cross-reactivity of other flavivirus antibodies, such as dengue. As such, FDA, BARDA and CDC have coordinated support to develop tests that perform at least as well as the CDC MAC-ELISA. Two tests developed by commercial manufacturers with support from BARDA are now available under FDA EUA for use in private sector clinical laboratories (hospitals, large commercial laboratories). The first, InBios Zika Detect™ IgM Capture ELISA, does not require specialized equipment and can be performed in CLIA accredited laboratories with proficiency in ELISA procedures. As of June 2016, InBios has manufactured and distributed 5,486 kits (as of 6/16/17; each kit can test 28 specimens). The second assay, DiaSorin LIAISON® Zika Capture IgM assay, runs on a proprietary, automated, high volume instrument that can perform 24 tests an hour. Several large clinical laboratories are currently evaluating this assay for use this summer. Other tests, including some tests supported by BARDA, at least one test that uses a high throughput analyzer and two tests that may be performed without any

instrumentation, are in development and under review with FDA. Once authorized by FDA, these assays will add to the national testing capacity. Moreover, BARDA is supporting the advanced development of two point-of-care diagnostic tests that would allow for rapid results for the clinician and patient.

The Honorable Frank Pallone

1. HHS recently reported that ASPR has obligated $110.6 million of its fiscal year2017 Zika funds. How much funding does BARDA have remaining in 2017 for Zika preparation or response? Does BARDA have sufficient funds remaining to support these efforts for the remainder of fiscal year 2017?

   Of the $245 million in Zika supplemental funding that ASPR/BARDA received in the Zika Response and Preparedness Act (division B of Public Law 114-223), $8.257 million remains unobligated as of May 15, 2017. These remaining funds will be obligated before the end of the fiscal year. BARDA has sufficient funding to support all of FY2017 planned activities for Zika response and preparation

The Honorable Kathy Castor

1. Please provide an update on vaccine development and clinical trials.

   BARDA is working closely with HHS interagency partners [National Institutes of Health (NIH)/National Institute of Allergy and Infectious Diseases (NIAID), FDA, and CDC], DoD [Walter Reed Army Institute of Research (WRAIR)] and the pharmaceutical industry to accelerate the development of several Zika vaccines. In particular, BARDA is supporting the development of four Zika vaccines based on two different platform approaches: 1) whole virus inactivated vaccines with alum adjuvant (Takeda, Sanofi Pasteur and Instituto Butantan), and 2) mRNA-based gene delivery (Moderna Therapeutics). All three inactivated vaccine candidates are in preclinical development stages. Phase I/II clinical trials are planned in fall 2017 (Takeda) and late summer 2018 (Sanofi Pasteur). Instituto Butantan, located in Sao Paulo, Brazil, is receiving support for the development and preparation of Zika vaccine under good manufacturing practices that will enable clinical studies at a later date. Moderna Therapeutics is presently conducting a Phase I clinical trial across three sites in the United States. Enrollment continues and data is expected later this year. A larger Phase II clinical trial in Latin America is being planned by Moderna for late 2017.

2. Please provide the latest information on the Zika vaccine licensing agreement between the U.S. Army and Sanofi and any relevant details.

BARDA is not involved in a decision to provide a license to Sanofi. Licensure negotiations are between Sanofi Pasteur and DoD/WRAIR.

3. With many members of Congress, states and public health advocates worried that the Zika vaccine being developed at the Walter Reed Army Institute of Research with taxpayer dollars will be priced too high, how is the federal government working to ensure Sanofi, when/if a licensing agreement is made, will sell this taxpayer funded vaccine at an affordable price to federal and state governments and to consumers?

   BARDA is keenly aware of the issues related to affordable and fair pricing of the medical countermeasures it develops. Many of the products BARDA develops are also procured by BARDA, CDC, DoD and are on the open market. Thus, procurement contracts are negotiated to allow for the greatest savings to the U.S. taxpayer. However, the Zika vaccine contracts were executed for the sole purpose of development and not intended for procurement by the government at this time. BARDA employs a portfolio approach that awards multiple vaccine development contracts to increase the probability in making available a safe and effective Zika vaccine. However, this approach promotes competition between manufacturers, thus potentially yielding lower costs in the marketplace.

4. How has public health advice regarding Zika evolved over the past few years for young men and women? What do we know now that we did not before and what new information could be on the horizon?

   BARDA respectfully defers to CDC on public health advice.

5. When does each federal agency believe they will run out of money to respond properly to Zika, including vector control, surveillance, vaccine and diagnostics development/improvement and research?

   BARDA currently has sufficient funding to support initial clinical studies for investigational vaccine candidates and diagnostics. Existing funds will be obligated on or before September 30, 2017.